STIC Search Report
EIC 1700

STIC Database Tracking Number: 176095

TO: Ben Sackey
Location: Rem 5B31
Art Unit : 1626
January 13, 2006

Case Serial Number: 10/761986

From: Kathleen Fuller
Location: EIC 1700
REMSEN 4B28
Phone: 571/272-2505
Kathleen.Fuller@uspto.gov

Search Notes

FOR OFFICIAL USE ONLY

ACCESS DB # 176095

PLEASE PRINT CLEARLY

Ms Fuller

Scientific and Technical Information Center

SEARCH REQUEST FORM

Requester's Full Name: Ben Sackey Examiner #: 73489 Date: 1/10/06

Art Unit: 1626 Phone Number: 2-0704 Serial Number: 10/761,986

Location (Bldg/Room#): REM 5 B31 Mailbox #: _____ Results Format Preferred (circle): PAPER DISK

****

To ensure an efficient and quality search, please attach a copy of the cover sheet, claims, and abstract or fill out the following:

Title of Invention: _____

Inventors (please provide full names): _____

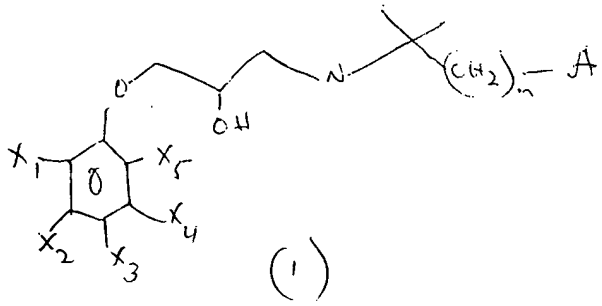
_____

Earliest Priority Date: _____

Search Topic:

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc., if known.

For Sequence Searches Only *Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*



(1)

A is aryl or fused aryl, dihydro, tetrahydro, etc.

$X_1 - X_5$ → H, halogen, CN and NO_2.

n is 0 – 4

Thanks

****

STAFF USE ONLY

Searcher: K. Fuller

Searcher phone #: _____

Searcher Location: _____

Date Searcher Picked Up: _____

Date Completed: 1/13/06

Searcher Prep & Review Time: 40

Online Time: 29

Type of Search

_____ NA Sequence (#)

_____ AA Sequence (#)

1 Structure (#)

_____ Bibliographic

_____ Litigation

_____ Fulltext

_____ Other

Vendors and cost where applicable

✓ STN _____ Dialog

_____ Questel/Orbit _____ Lexis/Nexis

_____ Westlaw _____ WWW/Internet

_____ In-house sequence systems

_____ Commercial _____ Oligomer _____ Score/Length

_____ Interference _____ SPDI _____ Encode/Transl

_____ Other (specify)

=> FILE REG
FILE 'REGISTRY' ENTERED AT 11:33:12 ON 13 JAN 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES: 11 JAN 2006 HIGHEST RN 871792-80-2
DICTIONARY FILE UPDATES: 11 JAN 2006 HIGHEST RN 871792-80-2

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2005

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

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**********************************************************************
*                                                                    *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added,    *
* effective March 20, 2005.  A new display format, IDERL, is now     *
* available and contains the CA role and document type information.  *
*                                                                    *
**********************************************************************
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Structure search iteration limits have been increased. See HELP SLIMITS
for details.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document. For information
on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

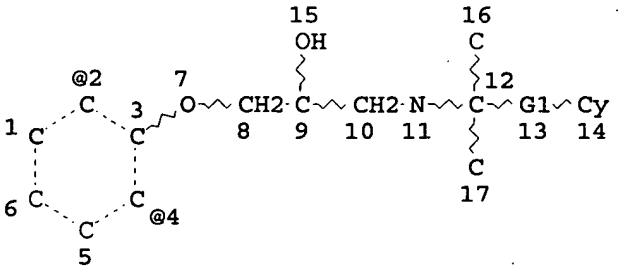
=> FILE HCAPLU
FILE 'HCAPLUS' ENTERED AT 11:33:17 ON 13 JAN 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 13 Jan 2006 VOL 144 ISS 4
FILE LAST UPDATED: 12 Jan 2006 (20060112/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> D QUE
L28 STR



600 structures from this query

G2 @18

REP G1=(0-4) CH2
VAR G2=X/CN/NO2
VPA 18-2/4 U
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 18

STEREO ATTRIBUTES: NONE

L30	600	SEA FILE=REGISTRY SSS FUL L28	
L33	149	SEA FILE=HCAPLUS ABB=ON	L30
L34	47	SEA FILE=HCAPLUS ABB=ON	L33(L)PREP/RL
L35	13	SEA FILE=HCAPLUS ABB=ON	L34 AND CALCILY?
L36	10	SEA FILE=HCAPLUS ABB=ON	L34 AND BONE?
L37	13	SEA FILE=HCAPLUS ABB=ON	L34 AND CALCIUM
L38	9	SEA FILE=HCAPLUS ABB=ON	L34 AND OSTEO?
L39	14	SEA FILE=HCAPLUS ABB=ON	(L35 OR L36 OR L37 OR L38)
L40	20	SEA FILE=HCAPLUS ABB=ON	L33 AND CALCILY?
L41	35	SEA FILE=HCAPLUS ABB=ON	L33 AND (BONE? OR OSTEO? OR CALCIUM)
L42	36	SEA FILE=HCAPLUS ABB=ON	L40 OR L41
L43	33	SEA FILE=HCAPLUS ABB=ON	L42 AND (PHARMACEU?/SC,SX OR THU/RL)
L44	34	SEA FILE=HCAPLUS ABB=ON	L39 OR L43

34 CA references with multiply

=> SEL HIT RN L44 1-34
E1 THROUGH E371 ASSIGNED too many RN's so printed only 1 per record

=> D L44 BIB ABS HITIND FHITSTR 1-34

L44 ANSWER 1 OF 34 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:1259579 HCAPLUS
DN 144:11601
TI Compositions and methods for modulating **bone** mass using β-adrenergic antagonists or agonists
IN Karsenty, Gerard; Devens, Bruce

PA Baylor College of Medicine, USA
SO PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005113012	A2	20051201	WO 2005-US16929	20050513

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2004-571558P P 20040514

AB The instant invention relates to compns. and methods for treating or preventing **bone** diseases. In certain aspects, the invention provides compns. comprising a β-adrenergic antagonist or agonist associated to a **bone**-targeted mol., as well as methods of modulating **bone** mass and/or growth in a mammal by administering a composition of the present invention. In other aspects, the invention provides methods of modulating **bone** mass and/or growth in a mammal by administering a composition comprising a β2-selective adrenergic antagonist or agonist. Thus, the expression in **osteoblasts** of genes encoding known regulators of **osteoclast** differentiation following treatment with isoproterenol was analyzed. In wildtype (WT) **osteoblasts** isoproterenol increased nearly 20-fold the expression of Rank-l, a gene encoding a secreted mol. required for **osteoclast** differentiation. The induction of Rank-l expression by isoproterenol was not detected when Adrb2-/- **osteoblasts** were used, indicating that this function of the sympathetic nervous system requires the presence of β2-adrenergic receptors on **osteoblasts.** Isoproterenol treatment also increased the expression of Il6, a cytokine that has been shown to favor **osteoclast** differentiation. These effects of isoproterenol were specific as it did not affect the expression of **osteoprotegerin** (Opg), a gene that encodes a decoy receptor for RANK-L, of M-CSF or of other interleukins tested, such as IL2 or ILIα (data not shown).

IC ICM A61K047-48
ICS A61P019-00
CC 63-6 (**Pharmaceuticals**)
Section cross-reference(s): 1
ST adrenoceptor beta agonist antagonist conjugate **bone** disease
IT Sialoglycoproteins
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(BSP (**bone** sialoprotein), **bone** targeting moiety; compns. comprising β-adrenergic antagonists or agonists for treating or preventing **bone** diseases)
IT **Bone**, disease
(Paget's; compns. comprising β-adrenergic antagonists or agonists for treating or preventing **bone** diseases)
IT Functional groups
(alkoxycarbonyl groups; compns. comprising β-adrenergic

antagonists or agonists for treating or preventing **bone** diseases)

IT Alcohols, biological studies
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(amino, linker; compns. comprising β-adrenergic antagonists or agonists for treating or preventing **bone** diseases)

IT Chelating agents
(**bone** targeting moieties; compns. comprising β-adrenergic antagonists or agonists for treating or preventing **bone** diseases)

IT Estrogens
Osteopontin
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(**bone** targeting moiety; compns. comprising β-adrenergic antagonists or agonists for treating or preventing **bone** diseases)

IT **Osteonectin**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**bone** targeting peptide associated with; compns. comprising β-adrenergic antagonists or agonists for treating or preventing **bone** diseases)

IT Functional groups
(carbamoyl group; compns. comprising β-adrenergic antagonists or agonists for treating or preventing **bone** diseases)

IT Amide group
Bone, disease
Bone formation
Bone mineral density
Carbonyl group
Combination chemotherapy
Drug delivery systems
Drug targets
Osteomalacia
Osteoporosis
Periodontium, disease
Phosphate group
Sulfhydryl group
Sympathetic nervous system
(compns. comprising β-adrenergic antagonists or agonists for treating or preventing **bone** diseases)

IT Antibodies and Immunoglobulins
Carbohydrates, biological studies
Peptides, biological studies
Proteins
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(compns. comprising β-adrenergic antagonists or agonists for treating or preventing **bone** diseases)

IT **Bone**, disease
(demineralization, associated with periprosthetic **osteolysis**; compns. comprising β-adrenergic antagonists or agonists for treating or preventing **bone** diseases)

IT Amines, biological studies
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(diamines, linker; compns. comprising β-adrenergic antagonists or agonists for treating or preventing **bone** diseases)

IT Carboxylic acids, biological studies
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(hydroxy, linker; compns. comprising β-adrenergic antagonists or agonists for treating or preventing **bone** diseases)

IT **Bone**, disease

(hyperostosis; compns. comprising β-adrenergic antagonists or agonists for treating or preventing **bone** diseases)

IT Amino acids, biological studies
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(linker; compns. comprising β-adrenergic antagonists or agonists for treating or preventing **bone** diseases)

IT **Bone**, disease
(**osteochondrosis**; compns. comprising β-adrenergic antagonists or agonists for treating or preventing **bone** diseases)

IT **Bone**, disease
(**osteopenia**; compns. comprising β-adrenergic antagonists or agonists for treating or preventing **bone** diseases)

IT **Bone**, disease
(**osteopetrosis**; compns. comprising β-adrenergic antagonists or agonists for treating or preventing **bone** diseases)

IT **Bone**, disease
(**osteosclerosis**; compns. comprising β-adrenergic antagonists or agonists for treating or preventing **bone** diseases)

IT Amino acids, biological studies
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(phosphonic acid analogs, **bone** targeting moiety; compns. comprising β-adrenergic antagonists or agonists for treating or preventing **bone** diseases)

IT **Bone**, disease
(renal **osteodystrophy**; compns. comprising β-adrenergic antagonists or agonists for treating or preventing **bone** diseases)

IT Carbohydrates, biological studies
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(sugar aminophosphates, **bone** targeting moiety; compns. comprising β-adrenergic antagonists or agonists for treating or preventing **bone** diseases)

IT **Osteoblast**
(targeting of; compns. comprising β-adrenergic antagonists or agonists for treating or preventing **bone** diseases)

IT Functional groups
(thio ester group; compns. comprising β-adrenergic antagonists or agonists for treating or preventing **bone** diseases)

IT Adrenoceptor agonists
Adrenoceptor antagonists
(β-; compns. comprising β-adrenergic antagonists or agonists for treating or preventing **bone** diseases)

IT Adrenoceptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(β2, agonists and antagonists; compns. comprising β-adrenergic antagonists or agonists for treating or preventing **bone** diseases)

IT 36894-69-6
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(Labetalol; compns. comprising β-adrenergic antagonists or agonists for treating or preventing **bone** diseases)

IT 53-43-0, DHEA 60-54-8, Tetracycline 1461-15-0, Calcein 2809-21-4 7664-38-2D, Phosphoric acid, derivs. 9007-12-9, Calcitonin 10596-23-3, Clodronate 13598-36-2D, Phosphonic acid, alkylidenebis- derivs. 13598-36-2D, Phosphonic acid, tetra derivs. 36465-90-4D, Diphosphonic acid, derivs. 40391-99-9 57738-23-5 66376-36-1, Alendronate 75755-07-6 79778-41-9, Neridronate 89987-06-4, Tiludronate

96293-62-8D, Triphosphonic acid, derivs. 105462-24-6 114084-78-5, Ibandronate 118072-93-8, Zoledronate 124351-85-5, Cimadronate 145224-96-0
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(**bone** targeting moiety; compns. comprising β-adrenergic antagonists or agonists for treating or preventing **bone** diseases)

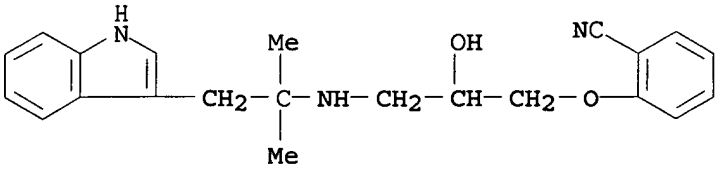
IT 169494-85-3D, Leptin, derivs.
RL: BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(combination with; compns. comprising β-adrenergic antagonists or agonists for treating or preventing **bone** diseases)

IT 525-66-6, Propranolol 1937-89-9, Butoxamine 2933-94-0, Toliprolol 3930-20-9, Sotalol 6452-71-7, Oxprenolol 6673-35-4, Practolol 7413-36-7, Nifenalol 7683-59-2, Isoproterenol 13523-86-9, Pindolol 13655-52-2, Alprenolol 14556-46-8, Bupranolol 18559-94-9, Salbutamol 22568-64-5, Diacetolol 22664-55-7, Metipranolol 23694-81-7, Mepindolol 26481-51-6, Tiprenolol 26839-75-8, Timolol 27325-36-6, Procinolol 27591-01-1, Bunolol 29122-68-7, Atenolol 34915-68-9, Bunitrolol 37517-30-9, Acebutolol 38363-40-5, Penbutolol 39552-01-7, Befunolol 39563-28-5, Cloranolol 39832-48-9, Tazolol 42200-33-9, Nadolol 47141-42-4, Levobunolol 51384-51-1, Metoprolol 51781-06-7, Carteolol 55837-19-9, Exaprolol 56980-93-9, Celiprolol 57775-29-8, Carazolol 58409-59-9, Bucumolol 58930-32-8, Butofilolol 59110-35-9, Pamatolol 59170-23-9, Bevantolol 60607-68-3, Indenolol 60979-28-4, IPS 339 62658-63-3, Bopindolol 63659-18-7, Betaxolol 66722-44-9, Bisoprolol 66848-46-2, Viskenit 68377-92-4, Arotinolol **71119-11-4**, Bucindolol 72795-19-8, ICI 118551 72956-09-3, Carvedilol 75659-07-3, Dilevalol 75949-60-9, Isoxaprolol 77164-20-6, Levomoprolol 81147-92-4, Esmolol 81447-80-5, Diprafenone 81801-12-9, Xamoterol 85320-68-9, Amosulalol 90055-97-3, Tienoxolol 90581-63-8, Falintolol 91277-57-5 94651-09-9, Cicloprolol 98418-47-4 102203-23-6, Acc 9369 114856-47-2, TZC-5665 115609-61-5, L-653328 118457-14-0, Nebivolol 125279-79-0, Ersentilide 132017-03-9, SR 58894A 153192-22-4, YM-430 153601-03-7, Capsinolol 165337-66-6, LM-2616 170684-14-7, UK 1745 174689-39-5, SR 59230A 188564-74-1, FR 172516 207922-70-1, CP 331684 264134-39-6, SB-226552 396712-03-1, AMO 140 396712-06-4, ISV 208
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(compns. comprising β-adrenergic antagonists or agonists for treating or preventing **bone** diseases)

IT 9028-35-7, NADPH-hydroxymethylglutaryl-CoA reductase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors, statins, combination with; compns. comprising β-adrenergic antagonists or agonists for treating or preventing **bone** diseases)

IT **71119-11-4**, Bucindolol
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(compns. comprising β-adrenergic antagonists or agonists for treating or preventing **bone** diseases)

RN 71119-11-4 HCAPLUS
CN Benzonitrile, 2-[2-hydroxy-3-[[2-(1H-indol-3-yl)-1,1-dimethylethyl]amino]propoxy]- (9CI) (CA INDEX NAME)



L44 ANSWER 2 OF 34 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:923021 HCAPLUS
DN 143:405677
TI Chemoenzymatic synthesis of **calcilytic** agent NPS-2143 employing a lipase-mediated resolution protocol
AU Kamal, Ahmed; Chouhan, Gagan
CS Biotransformations Laboratory, Division of Organic Chemistry, Indian Institute of Chemical Technology, Hyderabad, 500 007, India
SO Tetrahedron: Asymmetry (2005), 16(16), 2784-2789
CODEN: TASYE3; ISSN: 0957-4166
PB Elsevier B.V.
DT Journal
LA English
AB The kinetic resolution of (±)-3,2-Cl(NC)C6H3OCH2CH(OH)CH2Cl (I) has been successfully carried out via a lipase-mediated transesterification with vinyl acetate in organic as well as ionic liquid media to yield (R)-I and its (S)-acetate in high enantioselectivity. An enantioconvergent synthesis has also been achieved by a Mitsunobu esterification of a mixture of (R)-I and (S)-acetate in one pot to convert (R)-I to (S)-acetate. The (S)-Acetate was hydrolyzed by LiOH·H2O to give (R)-epoxide which was used as a chiral precursor for the synthesis of NPS-2143.
CC 25-24 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
IT Resolution (separation)
(enzymic; chemoenzymic synthesis of **calcilytic** agent NPS-2143 via lipase-mediated resolution of a cyanohydrin intermediate)
IT 867040-06-0P
RL: BPN (Biosynthetic preparation); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation)
(chemoenzymic synthesis of **calcilytic** agent NPS-2143 via lipase-mediated resolution of a cyanohydrin intermediate)
IT 867040-05-9P
RL: BPN (Biosynthetic preparation); RCT (Reactant); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(chemoenzymic synthesis of **calcilytic** agent NPS-2143 via lipase-mediated resolution of a cyanohydrin intermediate)
IT 79-46-9, 2-Nitropropane 106-89-8, Epichlorohydrin, reactions 448-61-3, 2,4,6-Triphenylpyrylium tetrafluoroborate 668-45-1, 2-Chloro-6-fluorobenzonitrile 2018-90-8, 2-Naphthalenemethanamine
RL: RCT (Reactant); RACT (Reactant or reagent)
(chemoenzymic synthesis of **calcilytic** agent NPS-2143 via lipase-mediated resolution of a cyanohydrin intermediate)
IT 89999-90-6P, 2-Chloro-6-hydroxybenzonitrile 198226-53-8P 198226-62-9P 198226-63-0P 400613-92-5P 867040-04-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(chemoenzymic synthesis of **calcilytic** agent NPS-2143 via lipase-mediated resolution of a cyanohydrin intermediate)
IT **284035-33-2P**, NPS-2143
RL: SPN (Synthetic preparation); **PREP (Preparation)**
(chemoenzymic synthesis of **calcilytic** agent NPS-2143 via

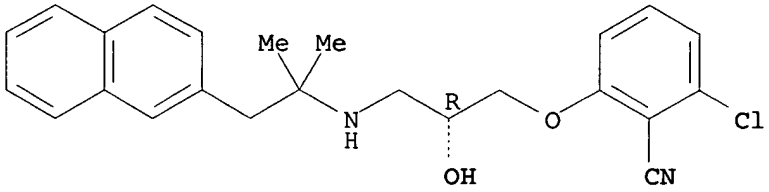
lipase-mediated resolution of a cyanohydrin intermediate)

IT **284035-33-2P**, NPS-2143
RL: SPN (Synthetic preparation); **PREP (Preparation)**
(chemoenzymic synthesis of **calcilytic** agent NPS-2143 via lipase-mediated resolution of a cyanohydrin intermediate)

RN 284035-33-2 HCAPLUS

CN Benzonitrile, 2-chloro-6-[(2R)-3-[[1,1-dimethyl-2-(2-naphthalenyl)ethyl]amino]-2-hydroxypropoxy]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L44 ANSWER 3 OF 34 HCAPLUS COPYRIGHT 2006 ACS on STN

AN 2005:902849 HCAPLUS

DN 143:229575

TI Preparation of amino-hydroxy-functionalized-aromatic carboxy compounds as **calcilytic** compounds useful against **bone** and mineral diseases

IN Marquis, Robert W., Jr.; Ramanjulu, Joshi M.

PA Smithkline Beecham Corporation, USA

SO PCT Int. Appl., 29 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005077892	A1	20050825	WO 2005-US3499	20050204

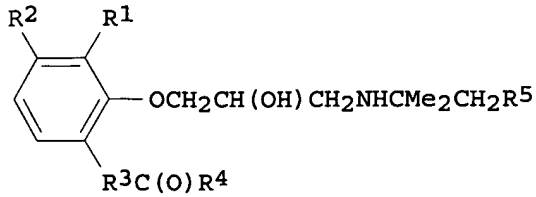
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2004-542554P P 20040206

OS MARPAT 143:229575

GI



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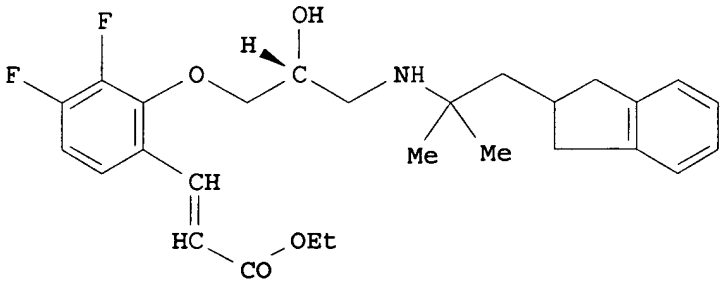


II

AB Novel **calcilytic** compds. (inhibitors of Ca receptor activity) (shown as I; R1 = H, CN, and halogen; R2 = H, halogen, CN, NO2, and SO2R4; R3 = (un)substituted C0-6 alkyl, and C0-6 alkenyl; R4 = OH, (un)substituted OC1-7alkyl; NH2, and NHR4; R5 = aryl, fused aryl, dihydro, tetrahydro fused aryl, and heteroaryl, (un)substituted with OH, halogen, C1-4 alkyl, C1-4 alkoxy, CF3, OCF3, CN and NO; e.g. (E)-3-[3,4-difluoro-2-[[(R)-2-hydroxy-3-[[2-(indan-2-yl)-1,1-dimethylethyl]amino]propyl]oxy]phenyl]-2-propenoic acid Et ester (shown as II)) and methods of using them are provided. No data is provided for the **calcilytic** activity of I. Although the methods of preparation are not claimed, 13 example prepns. are included. For example, II was prepared in 4 steps (18, 87, 80, and 82 % yields) starting with bromination of 2,3-difluorophenol and involving intermediates 6-bromo-2,3-difluorophenol, (R)-2-[(6-bromo-2,3-difluorophenoxy)methyl]oxirane, and (R)-1-(6-bromo-2,3-difluorophenoxy)-3-[[2-(indan-2-yl)-1,1-dimethylethyl]amino]propan-2-ol.

IC ICM C07C255-03
ICS C07C229-10

CC 25-19 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
Section cross-reference(s): 1, 2

ST arom carboxy compd amino alc prepn **calcilytic** compd; **bone** mineral disease drug arom carboxy compd amino alc

IT **Bone**, disease
(Paget's; preparation of amino-hydroxy-functionalized-aromatic carboxy compds. as **calcilytic** compds. useful against **bone** and mineral diseases)

IT Protein motifs
(SH2 domain, src SH2 antagonists, codrugs; preparation of amino-hydroxy-functionalized-aromatic carboxy compds. as **calcilytic** compds. useful against **bone** and mineral diseases)

IT **Bone**, disease
Bone minerals
(abnormal homeostasis; preparation of amino-hydroxy-functionalized-aromatic carboxy compds. as **calcilytic** compds. useful against **bone** and mineral diseases)

IT Alcohols, preparation
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); **THU**

(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(amino, aromatic, drug candidates; preparation of amino-hydroxy-functionalized-aromatic carboxy compds. as **calcilytic** compds. useful against **bone** and mineral diseases)

IT Vitronectin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antagonists, codrugs; preparation of amino-hydroxy-functionalized-aromatic carboxy compds. as **calcilytic** compds. useful against **bone** and mineral diseases)

IT Amides, preparation
Carboxylic acids, preparation
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(aromatic, drug candidates; preparation of amino-hydroxy-functionalized-aromatic carboxy compds. as **calcilytic** compds. useful against **bone** and mineral diseases)

IT Phosphonates
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(bisphosphonates, codrugs; preparation of amino-hydroxy-functionalized-aromatic carboxy compds. as **calcilytic** compds. useful against **bone** and mineral diseases)

IT Receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**calcium**, antagonists; preparation of amino-hydroxy-functionalized-aromatic carboxy compds. as **calcilytic** compds. useful against **bone** and mineral diseases)

IT **Bone** resorption inhibitors
Selective estrogen receptor modulators
(codrugs; preparation of amino-hydroxy-functionalized-aromatic carboxy compds. as **calcilytic** compds. useful against **bone** and mineral diseases)

IT Estrogens
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(codrugs; preparation of amino-hydroxy-functionalized-aromatic carboxy compds. as **calcilytic** compds. useful against **bone** and mineral diseases)

IT Carboxylic acids, preparation
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(esters, aromatic, drug candidates; preparation of amino-hydroxy-functionalized-aromatic carboxy compds. as **calcilytic** compds. useful against **bone** and mineral diseases)

IT Wound healing
Wound healing promoters
(fracture; preparation of amino-hydroxy-functionalized-aromatic carboxy compds. as **calcilytic** compds. useful against **bone** and mineral diseases)

IT Neoplasm
(humoral hypercalcemia of malignancy; preparation of amino-hydroxy-functionalized-aromatic carboxy compds. as **calcilytic** compds. useful against **bone** and mineral diseases)

IT **Bone**, neoplasm
Sarcoma
(**osteosarcoma**; preparation of amino-hydroxy-functionalized-aromatic carboxy compds. as **calcilytic** compds. useful against **bone** and mineral diseases)

IT Antiarthritics

Antirheumatic agents
Antitumor agents
Combination chemotherapy
Human
Osteoarthritis
Osteoporosis
Periodontium, disease
Rheumatoid arthritis
(preparation of amino-hydroxy-functionalized-aromatic carboxy compds. as **calcilytic** compds. useful against **bone** and mineral diseases)

IT Joint, anatomical
(replacement; preparation of amino-hydroxy-functionalized-aromatic carboxy compds. as **calcilytic** compds. useful against **bone** and mineral diseases)

IT 9000-83-3, ATPase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(V-H+-ATPase, inhibitors, codrugs; preparation of amino-hydroxy-functionalized-aromatic carboxy compds. as **calcilytic** compds. useful against **bone** and mineral diseases)

IT 7440-70-2, **Calcium**, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(abnormal homeostasis; preparation of amino-hydroxy-functionalized-aromatic carboxy compds. as **calcilytic** compds. useful against **bone** and mineral diseases)

IT 9007-12-9, Calcitonin 32222-06-3
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(codrug; preparation of amino-hydroxy-functionalized-aromatic carboxy compds. as **calcilytic** compds. useful against **bone** and mineral diseases)

IT **862992-86-7P**, (E)-3-[3,4-Difluoro-2-[[(R)-2-hydroxy-3-[[2-(indan-2-yl)-1,1-dimethylethyl]amino]propyl]oxy]phenyl]-2-propenoic acid ethyl ester **862992-89-0P**, 3-[3,4-Difluoro-2-[[(R)-2-hydroxy-3-[[2-(indan-2-yl)-1,1-dimethylethyl]amino]propyl]oxy]phenyl]propionic acid ethyl ester **862992-91-4P**, (E)-3-[3-Cyano-2-[[(R)-2-hydroxy-3-[[2-(indan-2-yl)-1,1-dimethylethyl]amino]propyl]oxy]phenyl]-2-propenoic acid ethyl ester **862992-96-9P**, 3-[3-Cyano-2-[[(R)-2-hydroxy-3-[[2-(indan-2-yl)-1,1-dimethylethyl]amino]propyl]oxy]phenyl]propionic acid ethyl ester **862992-98-1P 862992-99-2P**, 4-[3-Cyano-2-[[(R)-2-hydroxy-3-[[2-(indan-2-yl)-1,1-dimethylethyl]amino]propyl]oxy]phenyl]butyric acid methyl ester **862993-00-8P**, 4-[3-Cyano-2-[[(R)-2-hydroxy-3-[[2-(indan-2-yl)-1,1-dimethylethyl]amino]propyl]oxy]phenyl]butyric acid hydrochloride **862993-02-0P**, (E)-5-[3-Cyano-2-[[(R)-2-hydroxy-3-[[2-(indan-2-yl)-1,1-dimethylethyl]amino]propyl]oxy]phenyl]pent-4-enoic acid ethyl ester **862993-03-1P**, 5-[3-Cyano-2-[[(R)-2-hydroxy-3-[[2-(indan-2-yl)-1,1-dimethylethyl]amino]propyl]oxy]phenyl]pentanoic acid ethyl ester **862993-07-5P**, 4-[3-Cyano-2-[[(R)-2-hydroxy-3-[[2-(indan-2-yl)-1,1-dimethylethyl]amino]propyl]oxy]phenyl]butyric acid
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); **PREP (Preparation)**; RACT (Reactant or reagent); USES (Uses)
(drug candidate; preparation of amino-hydroxy-functionalized-aromatic carboxy compds. as **calcilytic** compds. useful against **bone** and mineral diseases)

IT **862992-90-3P**, 3-[3,4-Difluoro-2-[[(R)-2-hydroxy-3-[[2-(indan-2-yl)-1,1-dimethylethyl]amino]propyl]oxy]phenyl]propionic acid **862992-97-0P**, 3-[3-Cyano-2-[[(R)-2-hydroxy-3-[[2-(indan-2-yl)-1,1-dimethylethyl]amino]propyl]oxy]phenyl]propionic acid hydrochloride **862993-01-9P**, 4-[3-Cyano-2-[[(R)-2-hydroxy-3-[[2-(indan-2-yl)-1,1-

dimethylethyl]amino]propyl]oxy]phenyl]butyric acid ethyl ester hydrochloride **862993-04-2P**, 5-[3-Cyano-2-[[(R)-2-hydroxy-3-[[2-(indan-2-yl)-1,1-dimethylethyl]amino]propyl]oxy]phenyl]pentanoic acid **862993-05-3P**, 5-[3-Cyano-2-[[(R)-2-hydroxy-3-[[2-(indan-2-yl)-1,1-dimethylethyl]amino]propyl]oxy]phenyl]pentanoic acid trifluoroacetate **862993-06-4P**, 3-[3-Cyano-2-[[(R)-2-hydroxy-3-[[2-(indan-2-yl)-1,1-dimethylethyl]amino]propyl]oxy]phenyl]propionic acid **862993-08-6P**, 4-[3-Cyano-2-[[(R)-2-hydroxy-3-[[2-(indan-2-yl)-1,1-dimethylethyl]amino]propyl]oxy]phenyl]butyric acid ethyl ester
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(drug candidate; preparation of amino-hydroxy-functionalized-aromatic carboxy compds. as **calcilytic** compds. useful against **bone** and mineral diseases)

IT 94716-09-3, Cathepsin K
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors, codrugs; preparation of amino-hydroxy-functionalized-aromatic carboxy compds. as **calcilytic** compds. useful against **bone** and mineral diseases)

IT 9002-64-6, Parathyroid hormone
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(method for increasing serum levels; preparation of amino-hydroxy-functionalized-aromatic carboxy compds. as **calcilytic** compds. useful against **bone** and mineral diseases)

IT 100-39-0, Benzyl bromide 140-88-5, Ethyl acrylate 1968-40-7 2975-41-9, Indan-2-ylamine 3724-55-8, Methyl 3-butenoate 6418-38-8, 2,3-Difluorophenol 28165-47-1, 3-Bromosalicylamide 115314-17-5, (2R)-Glycidyl 3-nitrobenzenesulfonate
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of amino-hydroxy-functionalized-aromatic carboxy compds. as **calcilytic** compds. useful against **bone** and mineral diseases)

IT 13073-28-4P, 3-Bromo-2-hydroxybenzonitrile 186590-23-8P, 6-Bromo-2,3-difluorophenol 862992-87-8P, (R)-2-[(6-Bromo-2,3-difluorophenoxy)methyl]oxirane **862992-88-9P**, (R)-1-(6-Bromo-2,3-difluorophenoxy)-3-[[2-(indan-2-yl)-1,1-dimethylethyl]amino]propan-2-ol 862992-92-5P, 2-Benzyloxy-3-bromobenzamide 862992-93-6P, 2-Benzyloxy-3-bromobenzonitrile 862992-94-7P, 3-Bromo-2-((R)-oxiranylmethoxy)benzonitrile **862992-95-8P**, 3-Bromo-2-[[(R)-2-hydroxy-3-[[2-(indan-2-yl)-1,1-dimethylethyl]amino]propyl]oxy]benzonitrile
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(preparation of amino-hydroxy-functionalized-aromatic carboxy compds. as **calcilytic** compds. useful against **bone** and mineral diseases)

IT 141349-89-5, Gene src kinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(src SH2 antagonists, codrugs; preparation of amino-hydroxy-functionalized-aromatic carboxy compds. as **calcilytic** compds. useful against **bone** and mineral diseases)

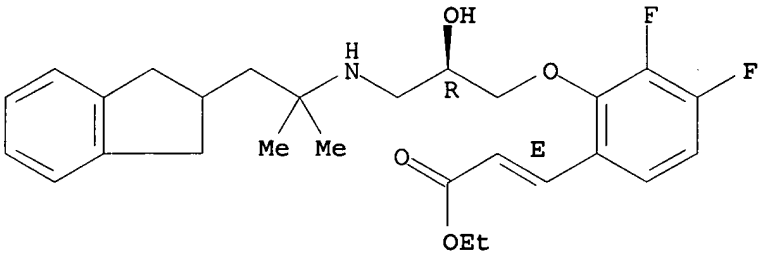
IT **862992-86-7P**, (E)-3-[3,4-Difluoro-2-[[(R)-2-hydroxy-3-[[2-(indan-2-yl)-1,1-dimethylethyl]amino]propyl]oxy]phenyl]-2-propenoic acid ethyl ester
RL: PAC (Pharmacological activity); RCT (Reactant); **PREP (Preparation)**; **THU (Therapeutic use)**; **PREP (Preparation)**; **PREP (Preparation)**; RACT (Reactant or reagent); USES (Uses)
(drug candidate; preparation of amino-hydroxy-functionalized-aromatic carboxy

compds. as **calcilytic** compds. useful against **bone** and mineral diseases)

RN 862992-86-7 HCAPLUS

CN 2-Propenoic acid, 3-[2-[(2R)-3-[[2-(2,3-dihydro-1H-inden-2-yl)-1,1-dimethylethyl]amino]-2-hydroxypropoxy]-3,4-difluorophenyl]-, ethyl ester, (2E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 4 OF 34 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:902847 HCAPLUS
DN 143:229574
TI Preparation of acyloxy-amino-functionalized-aromatic carboxy compounds as **calcilytic** compounds useful against **bone** and mineral diseases
IN Marquis, Robert W., Jr.; Ramanjulu, Joshi M.; Casillas, Linda N.
PA Smithkline Beecham Corporation, USA
SO PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005077886	A1	20050825	WO 2005-US3500	20050204

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2004-542763P P 20040206
OS MARPAT 143:229574
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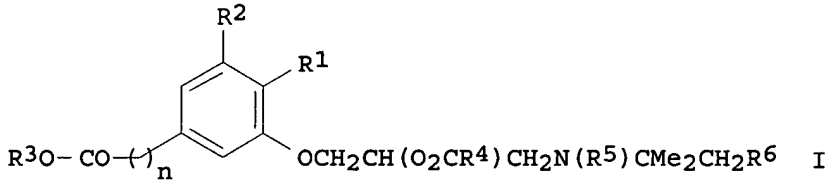

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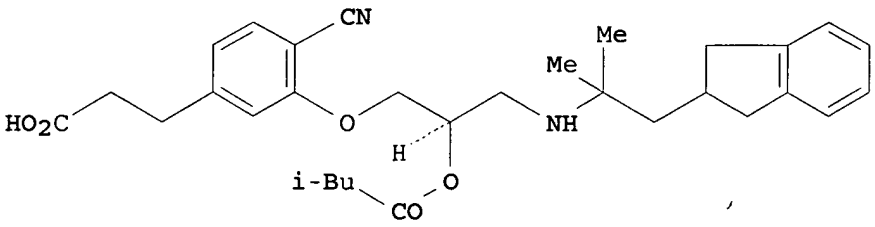


II

AB Novel **calcilytic** compds. (inhibitors of Ca receptor activity) (shown as I; R1 = H, CN, and halogen; R2 = halogen and H; R3 = H and (un)substituted C1-5 alkyl; n = 0-5; R4 = C1-7 alkyl and cycloalkyl; R5 is H or COR4; and R6 = aryl, fused aryl, dihydro, tetrahydro fused aryl, and heteroaryl, (un)substituted with OH, halogen, C1-4 alkyl, C1-4 alkoxy, CF,, OCF3, CN and NO2; e.g. 3-[4-cyano-3-[[(2R)-3-[[2-(2,3-dihydro-1H-inden-2-yl)-1,1-dimethylethyl]amino]-2-[(3-methylbutanoyl)oxy]propyl]oxy]phenyl]propanoic acid hydrochloride (free base shown as II)) and methods of using them are provided. No data is provided for the **calcilytic** activity of I. Although the methods of preparation are not claimed, 23 example prepns. are included. For example, II was prepared in 1 step (20 % yield) from 3-[4-cyano-3-[[(2R)-3-[[2-(2,3-dihydro-1H-inden-2-yl)-1,1-dimethylethyl]amino]-2-hydroxypropyl]oxy]phenyl]propanoic acid and isovaleric anhydride followed by HCl treatment.

IC ICM C07C229-00
ICS C07C069-74; C07C069-02

CC 25-19 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
Section cross-reference(s): 1, 2

ST arom carboxy compd acyloxy amino prepn **calcilytic** compd; **bone** mineral disease drug arom carboxy compd acyloxy amino; **calcium** abnormal homeostasis drug arom carboxy compd acyloxy amino

IT **Bone**, disease
(Paget's; preparation of acyloxy-amino-functionalized-aromatic carboxy compds. as **calcilytic** compds. useful against **bone** and mineral diseases)

IT Protein motifs
(SH2 domain, src SH2 antagonists, codrugs; preparation of acyloxy-amino-functionalized-aromatic carboxy compds. as **calcilytic** compds. useful against **bone** and mineral diseases)

IT **Bone**, disease
Bone minerals
(abnormal homeostasis; preparation of acyloxy-amino-functionalized-aromatic carboxy compds. as **calcilytic** compds. useful against **bone** and mineral diseases)

IT Vitronectin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antagonists, codrugs; preparation of acyloxy-amino-functionalized-aromatic carboxy compds. as **calcilytic** compds. useful against **bone** and mineral diseases)

IT Carboxylic acids, preparation
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(aromatic, drug candidates; preparation of acyloxy-amino-functionalized-aromatic carboxy compds. as **calcilytic** compds. useful against **bone** and mineral diseases)

IT Phosphonates
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(bisphosphonates, codrugs; preparation of acyloxy-amino-functionalized-aromatic carboxy compds. as **calcilytic** compds. useful against **bone** and mineral diseases)

IT Receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**calcium**, antagonists; preparation of acyloxy-amino-functionalized-aromatic carboxy compds. as **calcilytic** compds. useful against **bone** and mineral diseases)

IT **Bone** resorption inhibitors
Selective estrogen receptor modulators
(codrugs; preparation of acyloxy-amino-functionalized-aromatic carboxy compds. as **calcilytic** compds. useful against **bone** and mineral diseases)

IT Estrogens
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(codrugs; preparation of acyloxy-amino-functionalized-aromatic carboxy compds. as **calcilytic** compds. useful against **bone** and mineral diseases)

IT Carboxylic acids, preparation
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(esters, aromatic, drug candidates; preparation of acyloxy-amino-functionalized-aromatic carboxy compds. as **calcilytic** compds. useful against **bone** and mineral diseases)

IT Wound healing
(fracture, humoral hypercalcemia associated with; preparation of acyloxy-amino-functionalized-aromatic carboxy compds. as **calcilytic** compds. useful against **bone** and mineral diseases)

IT Wound healing promoters
(fracture; preparation of acyloxy-amino-functionalized-aromatic carboxy compds. as **calcilytic** compds. useful against **bone** and mineral diseases)

IT Neoplasm
(humoral hypercalcemia of malignancy; preparation of acyloxy-amino-functionalized-aromatic carboxy compds. as **calcilytic** compds. useful against **bone** and mineral diseases)

IT **Bone**, neoplasm
Sarcoma
(**osteosarcoma**; preparation of acyloxy-amino-functionalized-aromatic carboxy compds. as **calcilytic** compds. useful against **bone** and mineral diseases)

IT Antiarthritics
Antirheumatic agents
Antitumor agents
Combination chemotherapy
Human
Osteoarthritis
Osteoporosis
Periodontium, disease

Rheumatoid arthritis
(preparation of acyloxy-amino-functionalized-aromatic carboxy compds. as **calcilytic** compds. useful against **bone** and mineral diseases)

IT Joint, anatomical
(replacement; preparation of acyloxy-amino-functionalized-aromatic carboxy compds. as **calcilytic** compds. useful against **bone** and mineral diseases)

IT 9000-83-3, ATPase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(V-H+-ATPase, inhibitors, codrugs; preparation of acyloxy-amino-functionalized-aromatic carboxy compds. as **calcilytic** compds. useful against **bone** and mineral diseases)

IT 9007-12-9, Calcitonin 32222-06-3
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(codrug; preparation of acyloxy-amino-functionalized-aromatic carboxy compds. as **calcilytic** compds. useful against **bone** and mineral diseases)

IT 863016-21-1P, Ethyl 3-[3-[[(2R)-2-(acetyloxy)-3-[[2-(2,3-dihydro-1H-inden-2-yl)-1,1-dimethylethyl]amino]propyl]oxy]-4-cyanophenyl]propanoate hydrochloride
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug candidate; preparation of acyloxy-amino-functionalized-aromatic carboxy compds. as **calcilytic** compds. useful against **bone** and mineral diseases)

IT 863016-05-1P, 3-[4-Cyano-3-[[(2R)-3-[[2-(2,3-dihydro-1H-inden-2-yl)-1,1-dimethylethyl]amino]-2-[(3-methylbutanoyl)oxy]propyl]oxy]phenyl]propanoic acid hydrochloride 863016-06-2P, 3-[4-Cyano-3-[[(2R)-3-[[2-(2,3-dihydro-1H-inden-2-yl)-1,1-dimethylethyl]amino]-2-[(2-methylpropanoyl)oxy]propyl]oxy]phenyl]propanoic acid hydrochloride 863016-07-3P, 3-[4-Cyano-3-[[(2R)-3-[[2-(2,3-dihydro-1H-inden-2-yl)-1,1-dimethylethyl]amino]-2-[(2,2-dimethylpropanoyl)oxy]propyl]oxy]phenyl]propanoic acid hydrochloride 863016-08-4P, 3-[3-[[(2R)-2-(Acetyloxy)-3-[[2-(2,3-dihydro-1H-inden-2-yl)-1,1-dimethylethyl]amino]propyl]oxy]-4-cyanophenyl]propanoic acid hydrochloride 863016-09-5P, 3-[4-Cyano-3-[[(2R)-2-[(cyclopropylcarbonyl)oxy]-3-[[2-(2,3-dihydro-1H-inden-2-yl)-1,1-dimethylethyl]amino]propyl]oxy]phenyl]propanoic acid hydrochloride 863016-12-0P, 3-[4-Cyano-3-[[(2R)-3-[[2-(2,3-dihydro-1H-inden-2-yl)-1,1-dimethylethyl]amino]-2-(D-valyloxy)propyl]oxy]phenyl]propanoic acid hydrochloride 863016-15-3P, 3-[3-[[(2R)-3-[[2-(2,3-Dihydro-1H-inden-2-yl)-1,1-dimethylethyl]amino]-2-[(3-methylbutanoyl)oxy]propyl]oxy]-4,5-difluorophenyl]propanoic acid trifluoroacetate 863016-19-7P, 3-[3-[[(2R)-3-[[2-(2,3-Dihydro-1H-inden-2-yl)-1,1-dimethylethyl]amino]-2-[(2-methylpropanoyl)oxy]propyl]oxy]-4,5-difluorophenyl]propanoic acid trifluoroacetate 863016-22-2P, Ethyl 3-[3-[[(2R)-3-[(acetyl)[2-(2,3-dihydro-1H-inden-2-yl)-1,1-dimethylethyl]amino]-2-(acetyloxy)propyl]oxy]-4-cyanophenyl]propanoate 863016-23-3P, (1R)-2-[[2-Cyano-5-[3-(ethyloxy)-3-oxopropyl]phenyl]oxy]-1-[[[2-(2,3-dihydro-1H-inden-2-yl)-1,1-dimethylethyl]amino]methyl]ethyl 2-methylpropanoate hydrochloride 863016-24-4P, (1R)-2-[[2-Cyano-5-[3-(ethyloxy)-3-oxopropyl]phenyl]oxy]-1-[[[2-(2,3-dihydro-1H-inden-2-yl)-1,1-dimethylethyl]amino]methyl]ethyl 3-methylbutanoate hydrochloride 863016-25-5P, (1R)-2-[[2-Cyano-5-[3-(ethyloxy)-3-oxopropyl]phenyl]oxy]-1-[[[2-(2,3-dihydro-1H-inden-2-yl)-1,1-dimethylethyl]amino]methyl]ethyl 2,2-dimethylpropanoate hydrochloride 863016-26-6P, (1R)-2-[[2-Cyano-5-[3-(ethyloxy)-3-oxopropyl]phenyl]oxy]-1-[[[2-(2,3-dihydro-1H-inden-2-yl)-1,1-dimethylethyl]amino]methyl]ethyl cyclopropanecarboxylate hydrochloride 863016-28-8P, Ethyl 3-[4-cyano-3-[[(2R)-3-[[2-(2,3-dihydro-1H-inden-2-yl)-1,1-

dimethylethyl]amino]-2-[(trifluoroacetyl)oxy]propyl]oxy]phenyl]propanoate 863016-29-9P, 3-[3-[[(2R)-3-[[2-(2,3-Dihydro-1H-inden-2-yl)-1,1-dimethylethyl]amino]-2-[(2,2-dimethylpropanoyl)oxy]propyl]oxy]-4,5-difluorophenyl]propanoic acid 863016-30-2P, 3-[3-[[(2R)-3-[[2-(2,3-Dihydro-1H-inden-2-yl)-1,1-dimethylethyl]amino]-2-[(2,2-dimethylpropanoyl)oxy]propyl]oxy]-4,5-difluorophenyl]propanoic acid trifluoroacetate 863016-31-3P, 3-[3-[[(2R)-3-[[2-(2,3-Dihydro-1H-inden-2-yl)-1,1-dimethylethyl]amino]-2-[(phenylcarbonyl)oxy]propyl]oxy]-4,5-difluorophenyl]propanoic acid hydrochloride 863016-32-4P, 3-[3-[[(2R)-2-(Acetyloxy)-3-[[2-(2,3-dihydro-1H-inden-2-yl)-1,1-dimethylethyl]amino]propyl]oxy]-4,5-difluorophenyl]propanoic acid 863016-33-5P, (1R)-2-[[2-(2,3-Dihydro-1H-inden-2-yl)-1,1-dimethylethyl]amino]-1-[[[5-[3-(ethyloxy)-3-oxopropyl]-2,3-difluorophenyl]oxy]methyl]ethyl 3-methylbutanoate hydrochloride 863016-35-7P, (1R)-2-[[2-(2,3-Dihydro-1H-inden-2-yl)-1,1-dimethylethyl]amino]-1-[[[5-[3-(ethyloxy)-3-oxopropyl]-2,3-difluorophenyl]oxy]methyl]ethyl 2-methylpropanoate 863016-36-8P, (1R)-2-[[2-(2,3-Dihydro-1H-inden-2-yl)-1,1-dimethylethyl]amino]-1-[[[5-[3-(ethyloxy)-3-oxopropyl]-2,3-difluorophenyl]oxy]methyl]ethyl 2,2-dimethylpropanoate 863016-37-9P, (1R)-2-[[2-(2,3-Dihydro-1H-inden-2-yl)-1,1-dimethylethyl]amino]-1-[[[5-[3-(ethyloxy)-3-oxopropyl]-2,3-difluorophenyl]oxy]methyl]ethyl benzoate 863016-38-0P, Ethyl 3-[3-[[(2R)-2-(acetyloxy)-3-[[2-(2,3-dihydro-1H-inden-2-yl)-1,1-dimethylethyl]amino]propyl]oxy]-4,5-difluorophenyl]propanoate 863016-40-4P, 3-[3-[[(2R)-3-[[2-(2,3-Dihydro-1H-inden-2-yl)-1,1-dimethylethyl]amino]-2-[(phenylcarbonyl)oxy]propyl]oxy]-4,5-difluorophenyl]propanoic acid 863016-41-5P, (1R)-2-[[2-(2,3-Dihydro-1H-inden-2-yl)-1,1-dimethylethyl]amino]-1-[[[5-[3-(ethyloxy)-3-oxopropyl]-2,3-difluorophenyl]oxy]methyl]ethyl 3-methylbutanoate
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of acyloxy-amino-functionalized-aromatic carboxy compds. as **calcilytic** compds. useful against **bone** and mineral diseases)

IT 94716-09-3, Cathepsin K
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors, codrugs; preparation of acyloxy-amino-functionalized-aromatic carboxy compds. as **calcilytic** compds. useful against **bone** and mineral diseases)

IT 9002-64-6, Parathyroid hormone
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(method for increasing serum levels; preparation of acyloxy-amino-functionalized-aromatic carboxy compds. as **calcilytic** compds. useful against **bone** and mineral diseases)

IT 79-30-1, Isobutyryl chloride 93-97-0, Benzoic anhydride 97-72-3, Isobutyric anhydride 108-12-3, Isovaleryl chloride 1468-39-9, Isovaleric anhydride 1538-75-6, 2,2,2-Trimethylacetic anhydride 1685-33-2, N-(Benzyloxycarbonyl)-D-Valine 3282-30-2, 2,2,2-Trimethylacetyl chloride 4023-34-1, Cyclopropanecarbonyl chloride **351490-27-2**, 3-[4-Cyano-3-[[(2R)-3-[[2-(2,3-dihydro-1H-inden-2-yl)-1,1-dimethylethyl]amino]-2-hydroxypropyl]oxy]phenyl]propanoic acid **702686-96-2**, 3-[3-[[(2R)-3-[[2-(2,3-Dihydro-1H-inden-2-yl)-1,1-dimethylethyl]amino]-2-hydroxypropyl]oxy]-4,5-difluorophenyl]propanoic acid hydrochloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of acyloxy-amino-functionalized-aromatic carboxy compds. as **calcilytic** compds. useful against **bone** and mineral diseases)

IT **351490-26-1P 863016-10-8P** 863016-11-9P 863016-13-1P

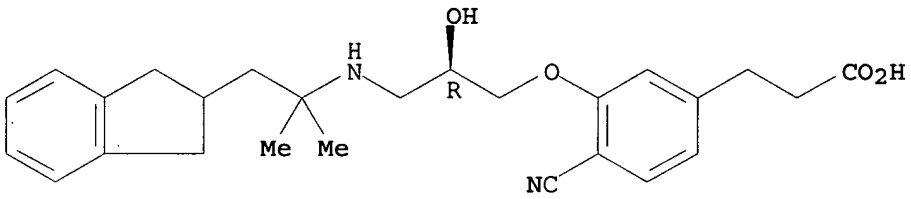
863016-16-4P 863016-17-5P 863016-20-0P **863016-34-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(preparation of acyloxy-amino-functionalized-aromatic carboxy compds. as **calcilytic** compds. useful against **bone** and mineral diseases)

IT 141349-89-5, Gene src kinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(src SH2 antagonists, codrugs; preparation of acyloxy-amino-functionalized-aromatic carboxy compds. as **calcilytic** compds. useful against **bone** and mineral diseases)

IT **351490-27-2**, 3-[4-Cyano-3-[[(2R)-3-[[2-(2,3-dihydro-1H-inden-2-yl)-1,1-dimethylethyl]amino]-2-hydroxypropyl]oxy]phenyl]propanoic acid
RL: RCT (Reactant); RACT (Reactant or reagent); **PREP (Preparation)**
(preparation of acyloxy-amino-functionalized-aromatic carboxy compds. as **calcilytic** compds. useful against **bone** and mineral diseases)

RN 351490-27-2 HCAPLUS
CN Benzenepropanoic acid, 4-cyano-3-[(2R)-3-[[2-(2,3-dihydro-1H-inden-2-yl)-1,1-dimethylethyl]amino]-2-hydroxypropoxy]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 5 OF 34 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:300430 HCAPLUS
DN 142:392445
TI A preparation of **calcilytic** compounds, useful as **calcium** receptor antagonists
IN Marquis, Robert W., Jr.
PA Glaxo Group Limited, UK
SO PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005030749	A1	20050407	WO 2004-US31120	20040923

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,

SN, TD, TG
PRAI US 2003-506001P P 20030924
OS MARPAT 142:392445
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to a preparation of novel **calcilytic** compds. of formula I [wherein: R1 is CN or halogen; R2 is H or halogen; R3 is (un)substituted alkyl or alkenyl; R4 is aryl, fused aryl, or heteroaryl, etc.], useful as **calcium** receptor antagonists. For instance, TFA salt of dioxabicyclopentadecatrienone derivative II was prepared via intramol. cyclization of hydroxycarboxylic acid III with a yield of 15%. Preferred invention compds. showed an IC50 of 10 μM or lower, and most preferred compds. showed an IC50 of 0.1 μM or lower.

IC ICM C07D313-00
ICS C07D321-00; A61K031-365; A61K031-335

CC 28-23 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, **63**

ST **calcilytic** compd prepn **calcium** receptor antagonist **osteosarcoma** antirheumatic malignancy; oxa bicyclopentadecatriene prepn **calcium** receptor antagonist

IT Proteins
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(ATPase inhibitor, anti-resorptive agent, drug component; preparation of **calcilytic** compound useful as **calcium** receptor antagonists)

IT Mammary gland, neoplasm
(Paget's disease, treatment of; preparation of **calcilytic** compound useful as **calcium** receptor antagonists)

IT **Bone**, disease
(Paget's, treatment of; preparation of **calcilytic** compound useful as **calcium** receptor antagonists)

IT Vitronectin receptors
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(anti-resorptive agent, antagonist of, drug component; preparation of **calcilytic** compound useful as **calcium** receptor antagonists)

IT Estrogens
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(anti-resorptive agent, drug component; preparation of **calcilytic** compound useful as **calcium** receptor antagonists)

IT Estrogen receptors
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(anti-resorptive agent, modulator of, drug component; preparation of **calcilytic** compound useful as **calcium** receptor antagonists)

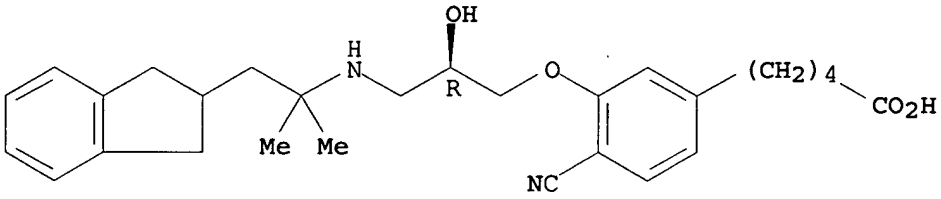
IT Homeostasis
(**bone** or mineral; preparation of **calcilytic** compound useful as **calcium** receptor antagonists)

IT Receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**calcium**, inhibitor; preparation of **calcilytic** compound useful as **calcium** receptor antagonists)

IT **Bone** resorption inhibitors
(drug component; preparation of **calcilytic** compound useful as **calcium** receptor antagonists)

IT Neoplasm
(humoral hypercalcemia of malignancy, treatment of; preparation of **calcilytic** compound useful as **calcium** receptor antagonists)
IT **Bone**, neoplasm
Sarcoma
(**osteosarcoma**, treatment of; preparation of **calcilytic** compound useful as **calcium** receptor antagonists)
IT Antirheumatic agents
Antitumor agents
Human
(preparation of **calcilytic** compound useful as **calcium** receptor antagonists)
IT Neoplasm
Osteoarthritis
Osteoporosis
Periodontium, disease
Rheumatoid arthritis
(treatment of; preparation of **calcilytic** compound useful as **calcium** receptor antagonists)
IT 67-97-0, Vitamin D3 9007-12-9, Calcitonin
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(anti-resorptive agent, drug component; preparation of **calcilytic** compound useful as **calcium** receptor antagonists)
IT 94716-09-3, Cathepsin K
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(anti-resorptive agent, inhibitor of, drug component; preparation of **calcilytic** compound useful as **calcium** receptor antagonists)
IT 7440-70-2, **Calcium**, biological studies
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(humoral hypercalcemia of malignancy treatment of; preparation of **calcilytic** compound useful as **calcium** receptor antagonists)
IT 849475-76-9P 849475-77-0P 849475-78-1P 849475-81-6P 849475-82-7P
849475-83-8P 849475-84-9P 849475-85-0P 849475-86-1P 849475-87-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of **calcilytic** compound useful as **calcium** receptor antagonists)
IT 818-57-5 113826-06-5 186590-26-1 **351490-67-0** 351490-85-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of **calcilytic** compound useful as **calcium** receptor antagonists)
IT **702686-98-4P 702686-99-5P** 702687-42-1P
702687-43-2P 849475-79-2P 849475-80-5P
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(preparation of **calcilytic** compound useful as **calcium** receptor antagonists)
IT **351490-67-0**
RL: RCT (Reactant); RACT (Reactant or reagent); **PREP (Preparation)**
(preparation of **calcilytic** compound useful as **calcium** receptor antagonists)
RN 351490-67-0 HCAPLUS
CN Benzenepentanoic acid, 4-cyano-3-[(2R)-3-[[2-(2,3-dihydro-1H-inden-2-yl)-1,1-dimethylethyl]amino]-2-hydroxypropoxy]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

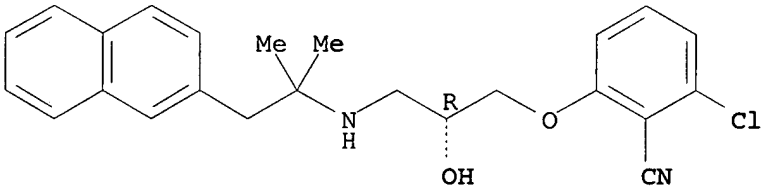


RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 6 OF 34 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:268991 HCAPLUS
DN 142:330127
TI A novel **calcium**-sensing receptor antagonist transiently stimulates parathyroid hormone secretion in vivo
AU Arey, Brian J.; Seethala, Ramakrishna; Ma, Zhengping; Fura, Aberra; Morin, Jennifer; Swartz, JoAnn; Vyas, Viral; Yang, Wu; Dickson, John K., Jr.; Feyen, Jean H. M.
CS Departments of Osteoporosis and Frailty, Pharmaceutical Research Institute, Bristol-Myers Squibb Company, Hopewell, NJ, 08534, USA
SO Endocrinology (2005), 146(4), 2015-2022
CODEN: ENDOAO; ISSN: 0013-7227
PB Endocrine Society
DT Journal
LA English
AB Circulating **calcium** (Ca2+) is a primary regulator of **bone** homeostasis through its action on PTH secretion. Extracellular Ca2+ modulates PTH secretion through a cell surface G protein-coupled receptor, the **calcium**-sensing receptor (CaR). The expression of the CaR suggests a critical role in cellular regulation by **calcium** in various organs, including parathyroid gland, **bone**, and kidney. Despite an obvious pharmacol. utility for CaR antagonists in the treatment of disease, only a limited number of such classes of compds. exist. We have identified a novel class of small mols. with specific activity at the CaR. This class of compds. is represented by compound 1. It possesses potent antagonist activity at the human CaR with IC50 values of 64 nM and 230 nM in inhibiting intracellular Ca2+ flux and inositol phosphate generation in vitro, resp. When administered to male rats in vivo, compound 1 robustly increased serum PTH levels. The stimulation of PTH secretion was rapid and transient when administered either iv or orally. The pharmacokinetic profile of compound 1 after oral administration revealed that maximal plasma levels of compound were reached within 1 h and the half-life of the compound to be approx. 2 h in rats. These data describe a representative compound of a novel chemical class than previously described allosteric modulators that offer a new avenue for the development of improved treatments of **osteoporosis.**
CC 2-7 (Mammalian Hormones)
ST **calcium** sensing receptor PTH NPS2143 analog PI3 kinase signaling
IT Biological transport
(**calcium**; novel **calcium**-sensing receptor antagonist transiently stimulates PTH secretion via PI3 kinase pathway)
IT Receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**calcium**; novel **calcium**-sensing receptor antagonist transiently stimulates PTH secretion via PI3 kinase pathway)
IT Biological transport
(influx, of **calcium**; novel **calcium**-sensing receptor

antagonist transiently stimulates PTH secretion via PI3 kinase pathway)
IT Human
Osteoporosis
Signal transduction, biological
(novel **calcium**-sensing receptor antagonist transiently stimulates PTH secretion via PI3 kinase pathway)
IT 7440-70-2, **Calcium**, biological studies 9002-64-6, Parathyroid hormone 15421-51-9, Inositol phosphate 115926-52-8, PI3 kinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(novel **calcium**-sensing receptor antagonist transiently stimulates PTH secretion via PI3 kinase pathway)
IT 802916-30-9
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); PKT (Pharmacokinetics); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(novel **calcium**-sensing receptor antagonist transiently stimulates PTH secretion via PI3 kinase pathway)
IT **284035-33-2**, NPS-2143
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(novel **calcium**-sensing receptor antagonist with similar structure of known NPS-2143, transiently stimulates PTH secretion via PI3 kinase pathway)
IT **284035-33-2**, NPS-2143
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(novel **calcium**-sensing receptor antagonist with similar structure of known NPS-2143, transiently stimulates PTH secretion via PI3 kinase pathway)
RN 284035-33-2 HCAPLUS
CN Benzonitrile, 2-chloro-6-[(2R)-3-[[1,1-dimethyl-2-(2-naphthalenyl)ethyl]amino]-2-hydroxypropoxy]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 7 OF 34 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:177840 HCAPLUS
DN 142:274011
TI Nitrosated and nitrosylated cardiovascular compounds, their compositions, and use
IN Garvey, David S.; Letts, Gordon L.; Worcel, Manuel; Gaston, Ricky D.
PA Nitromed, Inc., USA
SO PCT Int. Appl., 132 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005018561	A2	20050303	WO 2004-US26909	20040820

WO 2005018561 A3 20050721
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2003-496639P P 20030820
US 2003-496722P P 20030820
US 2003-496810P P 20030821
US 2003-498291P P 20030828
US 2003-498308P P 20030828
US 2003-530643P P 20031219

OS MARPAT 142:274011

AB Compns. and kits are described, comprising a nitrosated and/or nitrosylated cardiovascular compound, a nitric oxide donor compound and/or another therapeutic agent for treating cardiovascular diseases, renovascular diseases, diabetes, diseases resulting from oxidative stress, endothelial dysfunctions, diseases caused by endothelial dysfunctions, cirrhosis, pre-eclampsia, **osteoporosis**, and nephropathy. The nitrosated and/or nitrosylated cardiovascular compds. are preferably β-adrenergic antagonists, ACE inhibitors, anti-hyperlipidemic compds., or antithrombotic and vasodilator compds.

IC ICM A61K

CC 1-8 (Pharmacology)

IT Aneurysm
Antiarrhythmics
Anticholesteremic agents
Anticoagulants
Anticoagulants
Antidiabetic agents
Antihypertensives
Antioxidants
Atherosclerosis
Calcium channel blockers
Cardiovascular agents
Cardiovascular system, disease
Cell proliferation
Diabetes mellitus
Diuretics
Embolism
Hypercholesterolemia
Hypertension
Hypolipemic agents
Kidney, disease
Osteoporosis
Platelet aggregation
Platelet aggregation
Platelet aggregation inhibitors
Potassium channel blockers
Shock (circulatory collapse)
Thrombosis
Vasodilators
Wound
(nitrosated and nitrosylated cardiovascular compds., their compns., and

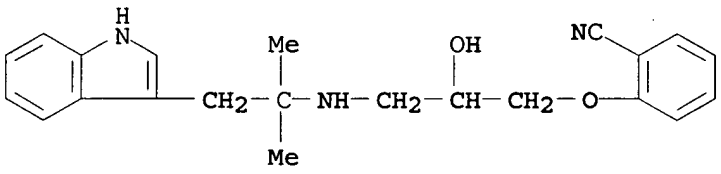
use)
IT 52-39-1, Aldosterone
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(antagonists; nitrosated and nitrosylated cardiovascular compds., their compns., and use)
IT 10102-43-9, Nitric oxide, biological studies
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(donor compds.; nitrosated and nitrosylated cardiovascular compds., their compns., and use)
IT 54-80-8D, Pronethalol, nitrosated and nitrosylated derivs. 58-93-5, Hydrochlorothiazide 77-36-1, Chlorthalidone 304-20-1, Hydralazine hydrochloride 318-98-9, Propranolol hydrochloride 396-01-0, Triamterene 525-66-6D, Propranolol, nitrosated and nitrosylated derivs. 2016-88-8, Amiloride hydrochloride 2933-94-0D, Toliprolol, nitrosated and nitrosylated derivs. 3930-20-9D, Sotalol, nitrosated and nitrosylated derivs. 5741-22-0D, Moprolol, nitrosated and nitrosylated derivs. 6452-71-7D, Oxprenolol, nitrosated and nitrosylated derivs. 6673-35-4D, Practolol, nitrosated and nitrosylated derivs. 7413-36-7D, Nifenalol, nitrosated and nitrosylated derivs. 13523-86-9D, Pindolol, nitrosated and nitrosylated derivs. 13655-52-2D, Alprenolol, nitrosated and nitrosylated derivs. 14556-46-8D, Bupranolol, nitrosated and nitrosylated derivs. 22664-55-7D, Metipranolol, nitrosated and nitrosylated derivs. 23694-81-7D, Mepindolol, nitrosated and nitrosylated derivs. 26839-75-8D, Timolol, nitrosated and nitrosylated derivs. 26921-17-5, Timolol maleate 29122-68-7D, Atenolol, nitrosated and nitrosylated derivs. 30187-90-7D, Xibenolol, nitrosated and nitrosylated derivs. 34915-68-9D, Bunitrolol, nitrosated and nitrosylated derivs. 34919-98-7D, Cetamolol, nitrosated and nitrosylated derivs. 36894-69-6D, Labetalol, nitrosated and nitrosylated derivs. 37517-30-9D, Acebutolol, nitrosated and nitrosylated derivs. 38363-40-5D, Penbutolol, nitrosated and nitrosylated derivs. 39552-01-7D, Befunolol, nitrosated and nitrosylated derivs. 39563-28-5D, Cloranolol, nitrosated and nitrosylated derivs. 42200-33-9D, Nadolol, nitrosated and nitrosylated derivs. 47141-42-4D, Levobunolol, nitrosated and nitrosylated derivs. 51384-51-1D, Metoprolol, nitrosated and nitrosylated derivs. 51781-06-7D, Carteolol, nitrosated and nitrosylated derivs. 53684-49-4D, Bufetolol, nitrosated and nitrosylated derivs. 54340-62-4D, Bufuralol, nitrosated and nitrosylated derivs. 56392-17-7, Metoprolol tartrate 56980-93-9D, Celiprolol, nitrosated and nitrosylated derivs. 57460-41-0D, Talinolol, nitrosated and nitrosylated derivs. 57775-29-8D, Carazolol, nitrosated and nitrosylated derivs. 58409-59-9D, Bucumolol, nitrosated and nitrosylated derivs. 58930-32-8D, Butofilolol, nitrosated and nitrosylated derivs. 59170-23-9D, Bevantolol, nitrosated and nitrosylated derivs. 60607-68-3D, Indenolol, nitrosated and nitrosylated derivs. 62571-86-2, Captopril 62571-86-2D, Captopril, nitrosated and nitrosylated derivs. 62658-63-3D, Bopindolol, nitrosated and nitrosylated derivs. 63659-18-7D, Betaxolol, nitrosated and nitrosylated derivs. 66264-77-5D, Sulfinalol, nitrosated and nitrosylated derivs. 66722-44-9D, Bisoprolol, nitrosated and nitrosylated derivs. 68377-92-4D, Arotinolol, nitrosated and nitrosylated derivs. **71119-11-4D**, Bucindolol, nitrosated and nitrosylated derivs. 72956-09-3, Carvedilol 72956-09-3D, Carvedilol, nitrosated and nitrosylated derivs. 74258-86-9D, Alacepril, nitrosated and nitrosylated derivs. 75659-07-3D, Dilevalol, nitrosated and nitrosylated derivs. 75847-73-3D, Enalapril, nitrosated and nitrosylated derivs. 76095-16-4, Enalapril maleate 76420-72-9D, Enalaprilat, nitrosated and nitrosylated derivs. 76547-98-3, Lisinopril 76547-98-3D, Lisinopril, nitrosated and nitrosylated derivs. 81147-92-4D, Esmolol, nitrosated and nitrosylated derivs. 81486-22-8D, Nipradilol, nitrosated and nitrosylated derivs. 82586-52-5, Moexipril

hydrochloride 82586-55-8, Quinapril hydrochloride 82834-16-0D, Perindopril, nitrosated and nitrosylated derivs. 83435-66-9D, Delapril, nitrosated and nitrosylated derivs. 83647-97-6D, Spirapril, nitrosated and nitrosylated derivs. 83688-84-0D, Tertatolol, nitrosated and nitrosylated derivs. 85136-71-6D, Tilisolol, nitrosated and nitrosylated derivs. 85320-68-9D, Amosulalol, nitrosated and nitrosylated derivs. 85441-61-8D, Quinapril, nitrosated and nitrosylated derivs. 85856-54-8D, Moveltipril, nitrosated and nitrosylated derivs. 86541-74-4, Benazepril hydrochloride 86541-75-5D, Benazepril, nitrosated and nitrosylated derivs. 87333-19-5D, Ramipril, nitrosated and nitrosylated derivs. 87679-37-6, Trandolapril 87679-37-6D, Trandolapril, nitrosated and nitrosylated derivs. 87679-71-8, Trandolaprilat 88768-40-5D, Cilazapril, nitrosated and nitrosylated derivs. 88889-14-9, Fosinopril sodium 89371-37-9D, Imidapril, nitrosated and nitrosylated derivs. 98048-97-6D, Fosinopril, nitrosated and nitrosylated derivs. 103775-10-6D, Moexipril, nitrosated and nitrosylated derivs. 104344-23-2, Bisoprolol fumarate 111223-26-8D, Ceronapril, nitrosated and nitrosylated derivs. 111902-57-9D, Temocapril, nitrosated and nitrosylated derivs. 124750-99-8, Losartan potassium 133242-30-5D, Landiolol, nitrosated and nitrosylated derivs. 137862-53-4, Valsartan 138402-11-6, Irbesartan 144143-96-4, Eprosartan mesylate 144689-63-4, Olmesartan medoxomil 144701-48-4, Telmisartan 145040-37-5, Candesartan Cilexetil
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(nitrosated and nitrosylated cardiovascular compds., their compns., and use)

IT **71119-11-4D**, Bucindolol, nitrosated and nitrosylated derivs.
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(nitrosated and nitrosylated cardiovascular compds., their compns., and use)

RN 71119-11-4 HCAPLUS

CN Benzonitrile, 2-[2-hydroxy-3-[[2-(1H-indol-3-yl)-1,1-dimethylethyl]amino]propoxy]- (9CI) (CA INDEX NAME)



L44 ANSWER 8 OF 34 HCAPLUS COPYRIGHT 2006 ACS on STN

AN 2005:108590 HCAPLUS

DN 142:216599

TI A Region in the Seven-transmembrane Domain of the Human Ca2+ Receptor Critical for Response to Ca2+

AU Hu, Jianxin; McLarnon, Stuart J.; Mora, Stefano; Jiang, Jiankang; Thomas, Craig; Jacobson, Kenneth A.; Spiegel, Allen M.

CS Molecular Pathophysiology Section, NIDCD, National Institutes of Health, Bethesda, MD, 20892, USA

SO Journal of Biological Chemistry (2005), 280(6), 5113-5120
CODEN: JBCHA3; ISSN: 0021-9258

PB American Society for Biochemistry and Molecular Biology

DT Journal

LA English

AB Of 12 naturally occurring, activating mutations in the seven-transmembrane (7TM) domain of the human Ca2+ receptor (CaR) identified previously in

subjects with autosomal dominant hypocalcemia (ADH), five appear at the junction of TM helixes 6 and 7 between residue Ile819 and Glu837. After identifying a sixth activating mutation in this region, V836L, in an ADH patient, the authors studied the remaining residues in this region to determine whether they are potential sites for activating mutations. Alanine-scanning mutagenesis revealed five addnl. residues in this region that when substituted by alanine led to CaR activation. The authors also found that, whereas E837A did not activate the receptor, E837D and E837K mutations did. Thus, region Ile819-Glu837 of the 7TM domain represents a "hot spot" for naturally occurring, activating mutations of the receptor, and most of the residues in this region apparently maintain the 7TM domain in its inactive configuration. Unique among the residues in this region, Pro823, which is highly conserved in family 3 of the G protein-coupled receptors, when mutated to either alanine or glycine, despite good expression severely impaired CaR activation by Ca2+. Both the P823A mutation and NPS 2143, a neg. allosteric modulator that acts on the 7TM through a critical interaction with Glu837, blocked activation of the CaR by various ADH mutations. These results suggest that the 7TM domain region Ile819-Glu837 plays a key role in CaR activation by Ca2+. The implications of the authors' finding that NPS 2143 corrects the mol. defect of ADH mutations for treatment of this disease are also discussed.

CC 14-14 (Mammalian Pathological Biochemistry)

ST **calcium** receptor transmembrane domain activating mutation autosomal dominant hypocalcemia

IT Receptors
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(**calcium**; region in seven-transmembrane domain of human Ca2+ receptor critical for response to Ca2+ in relation to activating mutations in autosomal dominant hypocalcemia)

IT 7440-70-2, **Calcium**, biological studies
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(autosomal dominant hypocalcemia; region in seven-transmembrane domain of human Ca2+ receptor critical for response to Ca2+ in relation to activating mutations in autosomal dominant hypocalcemia)

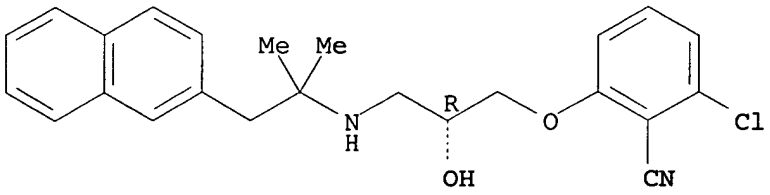
IT **284035-33-2**, NPS 2143
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(region in seven-transmembrane domain of human Ca2+ receptor critical for response to Ca2+ in relation to activating mutations in autosomal dominant hypocalcemia and)

IT **284035-33-2**, NPS 2143
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(region in seven-transmembrane domain of human Ca2+ receptor critical for response to Ca2+ in relation to activating mutations in autosomal dominant hypocalcemia and)

RN 284035-33-2 HCAPLUS

CN Benzonitrile, 2-chloro-6-[(2R)-3-[[1,1-dimethyl-2-(2-naphthalenyl)ethyl]amino]-2-hydroxypropoxy]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 9 OF 34 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:470952 HCAPLUS
DN 141:38435
TI Preparation of phenylalkanoic acids as **calcilytic** compounds
IN Marquis, Robert W.; Casillas, Linda N.; Ramanjulu, Joshi M.; Callahan, James Francis
PA Smithkline Beecham Corporation, USA
SO PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004047751	A2	20040610	WO 2003-US37461	20031125
	WO 2004047751	A3	20040819		
	W: AE, AG, AL, AU, BA, BB, BR, BZ, CA, CN, CO, CR, CU, DM, DZ, EC, EG, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, OM, PH, PL, RO, SC, SG, TN, TT, UA, US, UZ, VN, YU, ZA				
	RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2507226	AA	20040610	CA 2003-2507226	20031125
	EP 1569892	A2	20050907	EP 2003-783752	20031125
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	BR 2003016544	A	20051004	BR 2003-16544	20031125
	NO 2005003071	A	20050622	NO 2005-3071	20050622
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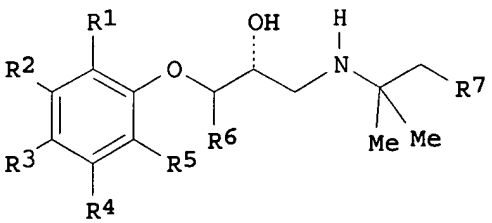
	WO 2003-US37461	W	20031125		

OS MARPAT 141:38435
GI



I

AB The title compds. I [R1, R5 = H, halo; R2 = R4 = H, halo, etc.; R6 = H, alkyl; R7 = aryl, fused aryl, etc.], useful as **calcilytics** (no data), are prepared Thus, I (R1 = R2 = F, R4 = CH:CHCO2H, R3 = H, R6 = H, R7 = indan-2-yl) was prepared by reaction of 5-bromo-2,3-difluorophenol with (2R)-glycidyl 3-nitrobenzenesulfonate followed by amination with 2-indan-2-yl-1,1-dimethylethy aryl substitution by Et acrylate followed by hydrolysis.

IC ICM A61K

CC 25-17 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
Section cross-reference(s): 1, **63**

ST phenylalkanoic acid prepn **calcilytic**

IT **Bone**, disease
(Paget's; preparation and potential uses of phenylalkanoic acids as **calcilytic** compds.)

IT **Bone**, disease
(fracture; preparation and potential uses of phenylalkanoic acids as **calcilytic** compds.)

IT **Bone**, neoplasm
Sarcoma
(**osteosarcoma**; preparation and potential uses of phenylalkanoic acids as **calcilytic** compds.)

IT Antiarthritics
Antirheumatic agents
Antitumor agents
Bone, disease
Drug delivery systems
Mammalia
Osteoarthritis
Osteoporosis
Periodontium, disease
Rheumatoid arthritis
(preparation and potential uses of phenylalkanoic acids as **calcilytic** compds.)

IT 7440-70-2, **Calcium**, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(hypercalcemia; preparation and potential uses of phenylalkanoic acids as **calcilytic** compds.)

IT 9002-64-6, Parathyroid hormone
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation and potential uses of phenylalkanoic acids as **calcilytic** compds.)

IT **702686-96-2P 702686-98-4P 702687-02-3P**
702687-07-8P 702687-08-9P 702687-11-4P
702687-17-0P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); **PREP (Preparation)**; RACT (Reactant or reagent); USES (Uses)
(preparation of phenylalkanoic acids as **calcilytic** compds.)

IT **702686-94-0P 702686-95-1P 702686-97-3P**
702686-99-5P 702687-00-1P 702687-03-4P
702687-04-5P 702687-05-6P 702687-06-7P
702687-09-0P 702687-10-3P 702687-13-6P
702687-14-7P 702687-16-9P 702687-19-2P
702687-20-5P 702687-21-6P 702687-22-7P 702687-23-8P
702687-24-9P 702687-25-0P 702687-26-1P 702687-27-2P
702687-28-3P 702687-29-4P 702687-30-7P 702687-31-8P 702687-32-9P
702687-33-0P 702687-34-1P 702687-35-2P **702687-37-4P**
702687-38-5P 702687-39-6P 702687-40-9P
702687-41-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); **THU**

(Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation of phenylalkanoic acids as **calcilytic** compds.)

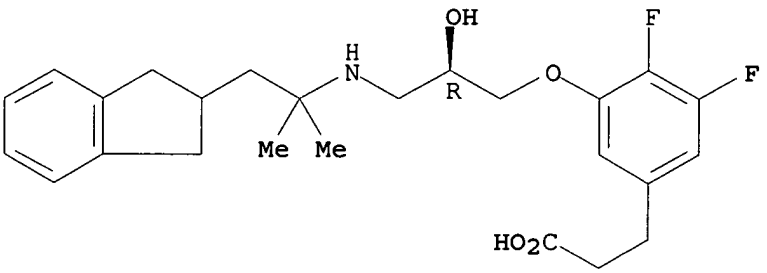
IT 140-88-5, Ethyl acrylate 621-54-5, 3-(3-Hydroxyphenyl)propionic acid 627-27-0, But-3-en-1-ol 1968-40-7, Ethyl 4-pentenoate 6418-38-8, 2,3-Difluorophenol 112204-58-7, 5-Bromo-2-fluorophenol 115314-17-5 144292-32-0 186590-26-1, 5-Bromo-2,3-difluorophenol 351490-85-2, 2-Indan-2-yl-1,1-dimethylethylamine 702687-66-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of phenylalkanoic acids as **calcilytic** compds.)

IT 1940-44-9P 34708-60-6P 702687-42-1P **702687-43-2P** 702687-44-3P 702687-45-4P **702687-46-5P** **702687-47-6P** **702687-48-7P** 702687-49-8P **702687-50-1P** **702687-51-2P** 702687-52-3P **702687-53-4P** **702687-54-5P** 702687-55-6P **702687-56-7P** **702687-57-8P** 702687-58-9P 702687-59-0P 702687-60-3P 702687-61-4P 702687-62-5P 702687-63-6P
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(preparation of phenylalkanoic acids as **calcilytic** compds.)

IT **702686-96-2P**
RL: PAC (Pharmacological activity); RCT (Reactant); **PREP (Preparation)**; **THU (Therapeutic use)**; **PREP (Preparation)**; **PREP (Preparation)**; RACT (Reactant or reagent); USES (Uses)
(preparation of phenylalkanoic acids as **calcilytic** compds.)

RN 702686-96-2 HCAPLUS
CN Benzenepropanoic acid, 3-[(2R)-3-[[2-(2,3-dihydro-1H-inden-2-yl)-1,1-dimethylethyl]amino]-2-hydroxypropoxy]-4,5-difluoro-, hydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

L44 ANSWER 10 OF 34 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:346555 HCAPLUS
DN 141:101805
TI Positive and Negative Allosteric Modulators of the Ca2+-sensing Receptor Interact within Overlapping but Not Identical Binding Sites in the Transmembrane Domain
AU Petrel, Christophe; Kessler, Albane; Dauban, Philippe; Dodd, Robert H.; Rognan, Didier; Ruat, Martial
CS UPR 9040 CNRS, Laboratoire de Neurobiologie Cellulaire et Moleculaire, IFR 2118 CNRS, the Institut de Neurobiologie Alfred Fessard, Gif sur Yvette,

91198, Fr.
SO Journal of Biological Chemistry (2004), 279(18), 18990-18997
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
AB A three-dimensional model of the human extracellular Ca2+-sensing receptor (CaSR) has been used to identify specific residues implicated in the recognition of two neg. allosteric CaSR modulators of different chemical structure, NPS 2143 and Calhex 231. To demonstrate the involvement of these residues, we have analyzed dose-inhibition response curves for the effect of these **calcilytics** on Ca2+-induced [3H]inositol phosphate accumulation for the selected CaSR mutants transiently expressed in HEK293 cells. These mutants were further used for investigating the binding pocket of two chemical unrelated pos. allosteric CaSR modulators, NPS R-568 and (R)-2-[1-(1-naphthyl)ethylaminomethyl]-1H-indole (Calindol), a novel potent calcimimetic that stimulates (EC50 = 0.31 μM) increases in [3H]inositol phosphate levels elicited by activating the wild-type CaSR by 2 mM Ca2+. Our data validate the involvement of Trp-8186.48, Phe-8216.51, Glu-8377.39, and Ile-8417.43 located in transmembranes (TM) 6 and TM7, in the binding pocket for both calcimimetics and **calcilytics**, despite important differences observed between each family of compds. The TMs involved in the recognition of both **calcilytics** include residues located in TM3 (Arg-6803.28, Phe-6843.32, and Phe-6883.36). However, our study indicates subtle differences between the binding of these two compds. Importantly, the observation that some mutations that have no effect on calcimimetics recognition but which affect the binding of **calcilytics** in TM3 and TM5, suggests that the binding pocket of pos. and neg. allosteric modulators is partially overlapping but not identical. Our CaSR model should facilitate the development of novel drugs of this important therapeutic target and the identification of the mol. determinants involved in the binding of allosteric modulators of class 3 G-protein-coupled receptors.
CC 6-3 (General Biochemistry)
Section cross-reference(s): 1, 13
ST allosteric modulator binding site **calcium** sensing receptor; calcimimetic **calcilytic** binding site **calcium** sensing receptor
IT Drugs
(calcimimetics and **calcilytics**; pos. and neg. allosteric modulators of Ca2+-sensing receptor (CaSR) interact within overlapping but not identical binding sites in transmembrane domain)
IT Receptors
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(**calcium**, CaSR (**calcium**-sensing receptor); pos. and neg. allosteric modulators of Ca2+-sensing receptor (CaSR) interact within overlapping but not identical binding sites in transmembrane domain)
IT Drug targets
(**calcium**-sensing receptor; pos. and neg. allosteric modulators of Ca2+-sensing receptor (CaSR) interact within overlapping but not identical binding sites in transmembrane domain)
IT 374933-30-9P, Calindol
RL: BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(pos. and neg. allosteric modulators of Ca2+-sensing receptor (CaSR) interact within overlapping but not identical binding sites in transmembrane domain)

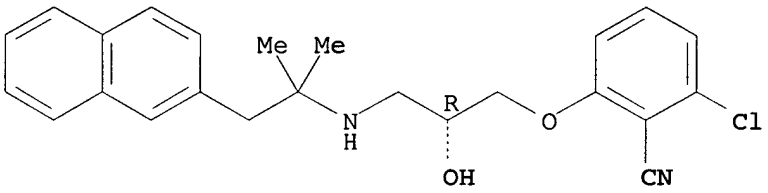
IT 177172-49-5, NPS R-568 **284035-33-2**, NPS 2143 652973-93-8, Calhex 231
RL: BSU (Biological study, unclassified); PRP (Properties); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(pos. and neg. allosteric modulators of Ca2+-sensing receptor (CaSR) interact within overlapping but not identical binding sites in transmembrane domain)

IT 7440-70-2, **Calcium**, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(signaling; pos. and neg. allosteric modulators of Ca2+-sensing receptor (CaSR) interact within overlapping but not identical binding sites in transmembrane domain)

IT **284035-33-2**, NPS 2143
RL: BSU (Biological study, unclassified); PRP (Properties); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(pos. and neg. allosteric modulators of Ca2+-sensing receptor (CaSR) interact within overlapping but not identical binding sites in transmembrane domain)

RN 284035-33-2 HCAPLUS
CN Benzonitrile, 2-chloro-6-[(2R)-3-[[1,1-dimethyl-2-(2-naphthalenyl)ethyl]amino]-2-hydroxypropoxy]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

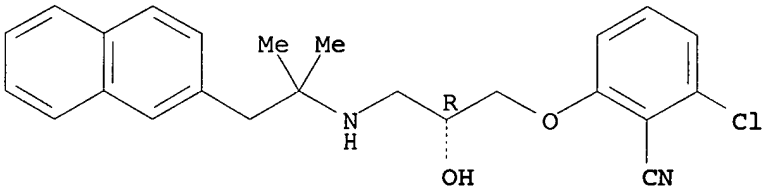


RE.CNT 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 11 OF 34 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:285983 HCAPLUS
DN 141:33149
TI **Calcium** receptor agonist (calcimimetics)
AU Nagano, Nobuo; Wada, Michihiro
CS Kirin Brewery Co., Ltd., Japan
SO Igaku no Ayumi (2004), 208(5), 285-290
CODEN: IGAYAY; ISSN: 0039-2359
PB Ishiyaku Shuppan
DT Journal; General Review
LA Japanese
AB A review. **Calcium** receptor agonist (calcimimetics) is reviewed including the pathol. of hyperparathyroidism and its treatment, **calcium** receptor antagonist (**calcilytics**) such as NPS2143, the role of parathyroidhormone (PTH) and **calcium** receptor as well as **calcium** receptor agonist (calcimimetics) such as cinacalcet hydrochloride in the treatment of hyperparathyroidism with examples.
CC 1-0 (Pharmacology)
ST review **calcium** receptor calcimimetic cinacalcet hydrochloride hyperparathyroidism
IT Hyperparathyroidism
(**calcium** receptor agonist (calcimimetics))
IT Receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**calcium**; **calcium** receptor agonist (calcimimetics))
IT 9002-64-6, Parathyroid hormone **284035-33-2**, NPS2143
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**calcium** receptor agonist (calcimimetics))
IT 364782-34-3, Cinacalcet hydrochloride
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(**calcium** receptor agonist (calcimimetics))
IT **284035-33-2**, NPS2143
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**calcium** receptor agonist (calcimimetics))
RN 284035-33-2 HCAPLUS
CN Benzonitrile, 2-chloro-6-[(2R)-3-[[1,1-dimethyl-2-(2-naphthalenyl)ethyl]amino]-2-hydroxypropoxy]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L44 ANSWER 12 OF 34 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:147870 HCAPLUS
DN 140:209771
TI Practical implications of drugs which improve survival versus those that reduce hospitalization and improve symptoms and quality of life in patients with heart failure due to reduced left ventricular systolic function
AU Thadani, U.
CS College of Medicine, Health Sciences Center and VA Medical Center, University of Oklahoma, Oklahoma City, OK, USA
SO Advances in Heart Failure, Proceedings of the World Congress on Heart Failure: Mechanisms and Management, 8th, Washington, DC, United States (2002), 343-350. Editor(s): Kimchi, Asher. Publisher: Medimond, Bologna, Italy.
CODEN: 69FBTG; ISBN: 88-323-2713-9
DT Conference; General Review
LA English
AB A review. Patients with heart failure (HF) due to reduced left ventricular (LV) systolic function (ejection fraction < 40%) have increased mortality and frequent hospitalizations due to decompensated HF. They also have reduced exercise tolerance and impaired quality of life due to dyspnea and fatigue. Pharmacotherapy for HF is targeted to reduce adverse clin. outcomes (death, hospitalization due to HF) and to improve the symptoms and quality of life. Diuretics reduce the symptoms and signs secondary to fluid retention and thus improve quality of life. Digoxin is the only inotropic agent that has a neutral effect on mortality, reduces HF hospitalizations and improves exercise performance. Other oral inotropic agents such as milrinone and vesnarinone increase morality in HF. Angiotensin converting enzyme inhibitors (ACE I), when added to digoxin and diuretics reduce death and HF hospitalizations in patients with NYHA class II - IV HF. Angiotensin (AT1) receptor blockers although not superior to ACE I's, are an excellent alternative in ACE intolerant

patients. Beta-blockers (bisoprolol, carvedilol, and metoprolol CR/XL but not bucindolol), significantly reduce mortality and HF hospitalizations when given in addition to digoxin, diuretics, and ACE I in patients with NYHA class II-IV HF. Aldosterone blocker, spironolactone when added to digoxin, diuretics and an ACE I reduces mortality in NYHA Class IV HF patients. Combination of an ACE I and AT1 receptor blocker, valsartan, in the absence of background beta-blocker therapy reduces HF hospitalizations. **Calcium** channel blockers, amlodipine and felodipine, when added to diuretics, digoxin and ACE inhibitors do not improve or worsen outcome in HF; other **calcium** channel blockers have a detrimental effect on mortality and morbidity. Lack of a beneficial effect or a possible detrimental effect was recently reported with an endothelin receptor blocker (bosentan), and with etanercept, and omapatrilat when given in addition to standard polytherapy for HF. Thus, multiple drugs have to be used to treat HF due to reduced LV function to reduce mortality, and hospitalizations due to decompensated HF and to relieve symptoms and improve quality of life.

CC 1-0 (Pharmacology)

IT Angiotensin receptor antagonists
Calcium channel blockers
Diuretics
Edema
Fatigue, biological
Human
Inotropics
(practical implications of drugs which improve survival vs. those that reduce hospitalization and improve symptoms and quality of life in patients with heart failure due to reduced left ventricular systolic function)

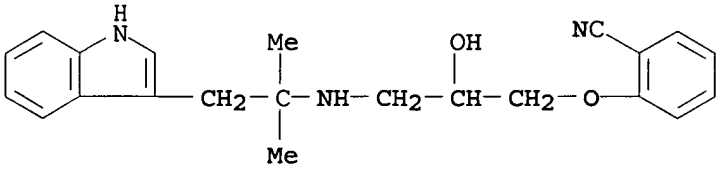
IT 78415-72-2, Milrinone 81840-15-5, Vesnarinone
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(practical implications of drugs which improve survival vs. those that reduce hospitalization and improve symptoms and quality of life in patients with heart failure due to reduced left ventricular systolic function)

IT 52-01-7, Spironolactone 20830-75-5, Digoxin 51384-51-1, Metoprolol 66722-44-9, Bisoprolol **71119-11-4**, Bucindolol 72509-76-3, Felodipine 72956-09-3, Carvedilol 88150-42-9, Amlodipine 137862-53-4, Valsartan 147536-97-8, Bosentan 167305-00-2, Omapatrilat 185243-69-0, Etanercept
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(practical implications of drugs which improve survival vs. those that reduce hospitalization and improve symptoms and quality of life in patients with heart failure due to reduced left ventricular systolic function)

IT **71119-11-4**, Bucindolol
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(practical implications of drugs which improve survival vs. those that reduce hospitalization and improve symptoms and quality of life in patients with heart failure due to reduced left ventricular systolic function)

RN 71119-11-4 HCAPLUS

CN Benzonitrile, 2-[2-hydroxy-3-[[2-(1H-indol-3-yl)-1,1-dimethylethyl]amino]propoxy]- (9CI) (CA INDEX NAME)



RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 13 OF 34 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:737573 HCAPLUS
DN 139:240367
TI Citalopram for the treatment of elevated blood pressure
IN Gabor, Pal S.
PA Egis Gyogyszergyar Rt., Hung.
SO PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003075914	A1	20030918	WO 2003-HU21	20030313
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2459834	AA	20030918	CA 2003-2459834	20030313
	BR 2003003384	A	20040330	BR 2003-3384	20030313
	EE 200400069	A	20040816	EE 2004-69	20030313
	EP 1490049	A1	20041229	EP 2003-743933	20030313
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	JP 2005519945	T2	20050707	JP 2003-574189	20030313
	ES 2238939	A1	20050901	ES 2004-50048	20030313
	LT 5255	B	20050825	LT 2004-49	20040512
	US 2005065209	A1	20050324	US 2004-489179	20041115
PRAI	HU 2002-980	A	20020314		
	WO 2003-HU21	W	20030313		

AB The invention relates to the use of citalopram or a pharmaceutically acceptable salt thereof for the preparation of pharmaceutical compns. suitable for the treatment of elevated (high) blood pressure, normalization of blood pressure or the decrease of elevated blood pressure and/or prevention of elevated blood pressure. Hypertensive patients were orally treated with citalopram in a dose of 5 mg/day on the first week, 10 mg/day on the second week and 20 mg/day on the third week. After the three weeks' treatment 47 patients (46 %) recovered and became normotensive. From the 55 non-responder patients, 40 individuals (39 %) received betaloc in an oral dose of 100 mg/day and 15 patients (15 %) received captopril in a dose of 2 x 12.5 mg/day, in addition to the administration of 20 mg/day of citalopram. After a six weeks treatment, complete recovery was experienced and the patients became normotensive.

IC ICM A61K031-343
ICS A61P009-12
CC 1-8 (Pharmacology)
IT **Calcium** channel blockers
Vasodilators
(as further antihypertensive agent; citalopram for treatment of high blood pressure)
IT 62571-86-2, Captopril
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(ACE inhibitor, as further antihypertensive agent; citalopram for treatment of high blood pressure)
IT 75847-73-3, Enalapril 76547-98-3, Lisinopril 82834-16-0, Perindopril 85441-61-8, Quinapril 86541-75-5, Benazepril 87333-19-5, Ramipril 87679-37-6, Trandolapril 98048-97-6, Fosinopril 103775-10-6, Moexipril
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(ACE inhibitor, as further antihypertensive agent; citalopram for treatment of high blood pressure)
IT 114798-26-4, Losartan 133040-01-4, Eprosartan 137862-53-4, Valsartan 138402-11-6, Irbesartan 139481-59-7, Candesartan 144701-48-4, Telmisartan
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(angiotensin II receptor antagonist, as further antihypertensive agent; citalopram for treatment of high blood pressure)
IT 56392-17-7, Betaloc
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(as further antihypertensive agent; citalopram for treatment of high blood pressure)
IT 555-30-6, Methyldopa 4205-90-7, Clonidine 5051-62-7, Guanabenz 29110-47-2, Guanfacine
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(as further antihypertensive agent; citalopram for treatment of high blood pressure)
IT 52-53-9, Verapamil 21829-25-4, Nifedipine 42399-41-7, Diltiazem 55985-32-5, Nicardipine 63675-72-9, Nisoldipine 66085-59-4, Nimodipine 72509-76-3, Felodipine 75695-93-1, Isradipine 88150-42-9, Amlodipine 103890-78-4, Lacidipine
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(**calcium** channel blocker, as further antihypertensive agent; citalopram for treatment of high blood pressure)
IT 59729-33-8, Citalopram
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(citalopram for treatment of high blood pressure)
IT 59729-33-8D, Citalopram, salts 128196-01-0, (S)-Citalopram
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(citalopram for treatment of high blood pressure)
IT 54187-04-1, Rilmenidine 75438-57-2, Moxonidine
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(imidazoline receptor agonist, as further antihypertensive agent; citalopram for treatment of high blood pressure)
IT 86-54-4, Hydralazine 364-98-7, Diazoxide 38304-91-5, Minoxidil 67227-56-9, Fenoldopam

RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(vasodilator, as further antihypertensive agent; citalopram for treatment of high blood pressure)

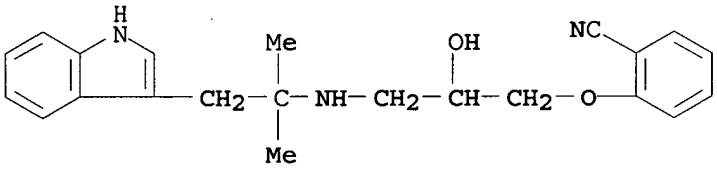
IT 50-60-2, Phentolamine 59-96-1, Phenoxybenzamine 19216-56-9, Prazosin 35795-16-5, Trimazosin 63590-64-7, Terazosin 74191-85-8, Doxazosin
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(α-blocker, as further antihypertensive agent; citalopram for treatment of high blood pressure)

IT 51384-51-1, Metoprolol
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(β-blocker, as further antihypertensive agent; citalopram for treatment of high blood pressure)

IT 525-66-6, Propranolol 13523-86-9, Pindolol 26839-75-8, Timolol 29122-68-7, Atenolol 36894-69-6, Labetalol 37517-30-9, Acebutolol 38363-40-5, Penbutolol 42200-33-9, Nadolol 51781-06-7, Carteolol 63659-18-7, Betaxolol 66722-44-9, Bisoprolol **71119-11-4**, Bucindolol 72956-09-3, Carvedilol 118457-14-0, Nebivolol
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(β-blocker, as further antihypertensive agent; citalopram for treatment of high blood pressure)

IT **71119-11-4**, Bucindolol
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(β-blocker, as further antihypertensive agent; citalopram for treatment of high blood pressure)

RN 71119-11-4 HCAPLUS
CN Benzonitrile, 2-[2-hydroxy-3-[[2-(1H-indol-3-yl)-1,1-dimethylethyl]amino]propoxy]- (9CI) (CA INDEX NAME)



RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 14 OF 34 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:319495 HCAPLUS
DN 138:343864
TI In vivo delivery methods and compositions
IN Kensey, Kenneth
PA USA
SO U.S. Pat. Appl. Publ., 45 pp., Cont.-in-part of U.S. Ser. No. 819,924.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 8

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003078517	A1	20030424	US 2001-839785	20010420
	US 6019735	A	20000201	US 1997-919906	19970828

CA	2301161	AA	19990304	CA 1998-2301161	19980826
NZ	502905	A	20010831	NZ 1998-502905	19980826
JP	2001514384	T2	20010911	JP 2000-507994	19980826
US	6322524	B1	20011127	US 1999-439795	19991112
US	6322525	B1	20011127	US 2000-501856	20000210
NO	2000000944	A	20000225	NO 2000-944	20000225
US	6428488	B1	20020806	US 2000-615340	20000712
WO	2002043806	A2	20020606	WO 2001-US44352	20011127
WO	2002043806	A3	20030327		
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	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
AU	2002026986	A5	20020611	AU 2002-26986	20011127
US	2002088953	A1	20020711	US 2001-33841	20011227
US	6624435	B2	20030923		
WO	2002079778	A2	20021010	WO 2002-US3984	20020207
WO	2002079778	A3	20030710		
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	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
US	2002184941	A1	20021212	US 2002-156165	20020528
US	6571608	B2	20030603		
PRAI US	1997-919906	A2	19970828		
US	1999-439795	A2	19991112		
US	2000-501856	A2	20000210		
US	2000-628401	A2	20000801		
US	2000-727950	B2	20001201		
US	2001-819924	A2	20010328		
US	1997-966076	A	19971107		
WO	1998-US17657	W	19980826		
US	2000-615340	A3	20000712		
US	2000-228612P	P	20000828		
US	2001-789350	B2	20010221		
US	2001-828761	A	20010409		
US	2001-839785	A	20010420		
US	2001-841389	A	20010424		
US	2001-897164	A3	20010702		
WO	2001-US44352	W	20011127		

AB Various methods are provided for determining and utilizing the viscosity of the circulating blood of a living being over a range of shear rates for diagnostics and treatment, such as detecting/reducing blood viscosity, work of the heart, contractility of the heart, for detecting/reducing the surface tension of the blood, for detecting plasma viscosity, for explaining/countering endothelial cell dysfunction, for providing high and low blood vessel wall shear stress data, red blood cell deformability data, lubricity of blood, and for treating different ailments such as

peripheral arterial disease in combination with administering to a living being at least 1 drug. Agents effective to regulate at least 1 of the aforementioned blood parameters are used to adjust distribution of a substance through the bloodstream.

IC ICM A61M031-00
ICS A61B005-02; A61B005-00; B65D081-00
INCL 600573000; 604066000; 604067000; 600504000
CC 63-6 (**Pharmaceuticals**)
Section cross-reference(s): 1
IT Hemoglobins
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(Hemosol; in vivo delivery methods and compns.)
IT Proteins
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(blood; in vivo delivery methods and compns.)
IT Clays, biological studies
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(colloidal; in vivo delivery methods and compns.)
IT Adrenoceptor antagonists
Agglutination
Animal tissue
Antiarrhythmics
Anticholesteremic agents
Anticoagulants
Antidiabetic agents
Antihypertensives
Antiobesity agents
Appetite depressants
Artery, disease
Blood
Blood coagulation
Calcium channel blockers
Electrolytes
Erythrocyte
Heart
Human
Hypolipemic agents
Lubricants
Organ, animal
Platelet aggregation
Platelet aggregation inhibitors
Shear
Shear stress
Surfactants
Thixotropy
Thrombus
Tobacco products
Vasodilators
Viscosity
(in vivo delivery methods and compns.)
IT Albumins, biological studies
Amino acids, biological studies
Antibodies and Immunoglobulins
Estrogens
Gelatins, biological studies
Minerals, biological studies
Polyoxyalkylenes, biological studies
Thrombomodulin
Vitamins
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)

(in vivo delivery methods and compns.)
IT Bentonite, biological studies
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(magnesium-treated; in vivo delivery methods and compns.)
IT Bentonite, biological studies
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(sodian; in vivo delivery methods and compns.)
IT 60202-16-6, Protein C
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(CTC 111; in vivo delivery methods and compns.)
IT 9041-08-1, OP 2000
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(OP 2000; in vivo delivery methods and compns.)
IT 65312-43-8, Blood-coagulation factor VIIa
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(eptacog alpha; in vivo delivery methods and compns.)
IT 50-28-2, Estradiol, biological studies 50-78-2, Aspirin 52-01-7, Spironolactone 52-53-9, Verapamil 54-11-5, Nicotine 54-31-9, Furosemide 55-63-0, Nitroglycerin 57-63-6, Ethinyl estradiol 57-83-0, Progestin, biological studies 58-32-2, Dipyridamole 58-54-8, Ethacrynic acid 58-93-5, Hydrochlorothiazide 58-94-6, Chlorothiazide 59-66-5, Acetazolamide 68-22-4, Norethindrone 69-65-8, Mannitol 70-51-9 72-33-3, Mestranol 81-81-2, Warfarin 86-54-4, Hydralazine 87-33-2, Isosorbide dinitrate 94-20-2, Chlorpropamide 122-09-8, Phentermine 396-01-0, Triamterene 520-85-4, Medroxyprogesterone 525-66-6, Propranolol 634-03-7, Phendimetrazine 637-07-0, Clofibrate 657-24-9, Metformin 797-63-7, Levonorgestrel 1156-19-0, Tolazamide 1231-93-2, Ethynodiol 2098-66-0, Cyproterone 3056-17-5, Stavudine 3930-20-9, Sotalol 4291-63-8, Cladribine 6533-00-2, Norgestrel 7631-86-9, Silicon dioxide, biological studies 8001-27-2, Hirudin 9000-69-5, Pectin 9000-94-6, Antithrombin III 9002-01-1, Streptokinase 9002-18-0, Agar 9002-72-6, Somatotropin 9004-10-8, Insulin, biological studies 9004-67-5, Methylcellulose 9005-27-0, Hetastarch 9007-12-9, Calcitonin 9039-53-6, Urokinase 10238-21-8, Glyburide 11041-12-6, Cholestyramine 12650-69-0, Mupirocin 13523-86-9, Pindolol 14808-79-8, Sulfate, biological studies 15291-77-7, Ginkgolide B 15307-86-5, Diclofenac 16051-77-7, Isosorbide mononitrate 17560-51-9, Metolazone 18559-94-9, Salbutamol 21256-18-8, Oxaprozin 21829-25-4, Nifedipine 24967-94-0, Dermatan sulfate 25322-68-3, Polyethylene glycol 25614-03-3, Bromocriptine 25812-30-0, Gemfibrozil 26807-65-8, Indapamide 26839-75-8, Timolol 28395-03-1, Bumetanide 28523-86-6, Sevoflurane 28721-07-5, Oxcarbazepine 29094-61-9, Glipizide 29122-68-7, Atenolol 29457-07-6, Ticarcillin disodium 30516-87-1, Zidovudine 32222-06-3, Calcitriol 34391-04-3, Levosalbutamol 34580-13-7, Ketotifen 34911-55-2, Bupropion 35189-28-7, Norgestimate 38304-91-5, Minoxidil 39562-70-4, Nitrendipine 42200-33-9, Nadolol 42399-41-7, Diltiazem 42924-53-8, Nabumetone 47141-42-4, Levobunolol 49562-28-9, Fenofibrate 50925-79-6, Colestipol 51333-22-3, Budesonide 51384-51-1, Metoprolol 54024-22-5, Desogestrel 55142-85-3, Ticlopidine 55985-32-5, Nicardipine 56180-94-0, Acarbose 56211-40-6, Torsemide 56420-45-2, Epirubicin 59122-46-2, Misoprostol 60282-87-3, Gestodene 62571-86-2, Captopril 63612-50-0, Nilutamide 63675-72-9, Nisoldipine 64221-86-9, Imipenem 64544-07-6, Cefuroxime axetil 64706-54-3, Bepridil 66085-59-4, Nimodipine 66722-44-9, Bisoprolol 67227-56-9, Fenoldopam 68252-19-7, Pirmenol 68291-97-4, Zonisamide 69655-05-6, Didanosine **71119-11-4**, Bucindolol 71486-22-1, Vinorelbine 72509-76-3, Felodipine 72956-09-3, Carvedilol 73573-87-2, Formoterol 73963-72-1, Cilostazol 74191-85-8, Doxazosin 74863-84-6, Argatroban 75330-75-5, Lovastatin 75695-93-1, Isradipine 75847-73-3, Enalapril 76547-98-3, Lisinopril 77191-36-7, Nefiracetam 78415-72-2, Milrinone

79350-37-1, Cefixime 79902-63-9, Simvastatin 80474-14-2, FLuticasone propionate 81732-65-2, Bambuterol 82410-32-0, Ganciclovir 83869-56-1, GM-CSF 84057-84-1, Lamotrigine 84057-95-4, Ropivacaine 84449-90-1, Raloxifene 84625-59-2, Dotarizine 85441-61-8, Quinapril 86541-75-5, Benazepril 86780-90-7, Aranidipine 87239-81-4, Cefpodoxime proxetil 87333-19-5, Ramipril 87679-37-6, Trandolapril 88150-42-9, Amlodipine 89565-68-4, Tropisetron 90729-41-2, Oxodipine 92665-29-7, Cefprozil 93221-48-8, Levobetaxolol 93479-97-1, Glimepiride 93957-54-1, Fluvastatin 94535-50-9, Lemakalim 94739-29-4, Lemildipine 95058-81-4, Gemcitabine 96036-03-2, Meropenem 96125-53-0, Clentiazem 96829-58-2, Orlistat 97240-79-4, Topiramate 97322-87-7, Troglitazone 97682-44-5, Irinotecan 98048-97-6, Fosinopril 99522-79-9, Pranidipine 100427-26-7, Lercanidipine 100986-85-4, Levofloxacin 101526-83-4, Sematilide 103577-45-3, Lansoprazole 103745-39-7, Fasudil 103890-78-4, Lacidipine 104713-75-9, Barnidipine 105816-04-4, Nateglinide 105857-23-6, Alteplase 105979-17-7, Benidipine 106650-56-0, Sibutramine 107452-89-1, Ziconotide 109889-09-0, Granisetron 111025-46-8, Pioglitazone 112809-51-5, Letrozole 113665-84-2, Clopidogrel 113806-05-6, Olopatadine 114432-13-2, Fantofarone 114798-26-4, Losartan 114870-03-0, Fondaparinux sodium 115103-54-3, Tiagabine 115256-11-6, Dofetilide 116308-55-5, Watanidipine 117279-73-9, Israpafant 118457-14-0, Nebivolol 119684-05-8, Mesoglycan 120511-73-1, Anastrozole 120993-53-5, Desirudin 121181-53-1, Filgrastim 121679-13-8, Naratriptan 122647-31-8, Ibutilide 123524-52-7, Azelnidipine 123774-72-1, Sargramostim 123948-87-8, Topotecan 124750-99-8, Losartan potassium 124832-26-4, Valacyclovir 124937-51-5, Tolterodine 128270-60-0, Bivalirudin 128470-16-6, Arbutamine 129618-40-2, Nevirapine 130209-82-4, Latanoprost 130636-43-0, Nifekalant 131179-95-8, RSR 13 132579-32-9, Rocepafant 132875-61-7, Remifentanil 133040-01-4, Eprosartan 133242-30-5, Landiolol 133652-38-7, Reteplase 134308-13-7, Tolcapone 134523-00-5, Atorvastatin 134678-17-4, Lamivudine 134865-37-5, Meluadrine tartrate 135062-02-1, Repaglinide 136468-36-5, Foropafant 137862-53-4, Valsartan 138068-37-8, Lepirudin 138402-11-6, Irbesartan 138661-03-7, Furnidipine 143653-53-6, Abciximab 144494-65-5, Tirofiban 144689-24-7, Olmesartan 144701-48-4, Telmisartan 145040-37-5, Candesartan cilexetil 145375-43-5, Mitiglinide 145599-86-6, Cerivastatin 147059-72-1, Trovafloxacin 147511-69-1, Pitavastatin 148883-56-1, Tifacogin 149908-53-2, Azimilide 150332-35-7, Pamaqueside 154189-24-9, ARC 68397AA 158876-82-5, Rupatadine 159776-70-2, Melagatran 170902-47-3, Roxifiban 173324-94-2, Temiverine 187523-35-9, BMS 204352 187741-48-6, CHF 1521 188627-80-7, Eptifibatide 192939-46-1, H376/95 210101-16-9, Conivaptan
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(in vivo delivery methods and compns.)

IT 679809-58-6, Enoxaparin sodium
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(in vivo delivery methods and compns.)

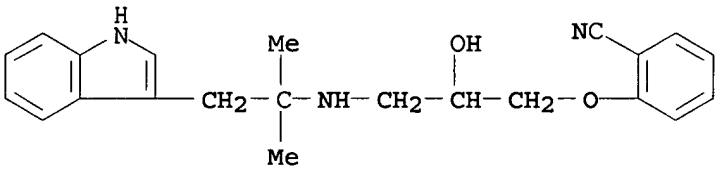
IT 9004-54-0, Dextran, biological studies
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(low mol. weight; in vivo delivery methods and compns.)

IT 9004-34-6, Cellulose, biological studies
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(microcryst.; in vivo delivery methods and compns.)

IT 9001-26-7, Prothrombin
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(rate; in vivo delivery methods and compns.)

IT **71119-11-4**, Bucindolol
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)

(in vivo delivery methods and compns.)
RN 71119-11-4 HCAPLUS
CN Benzonitrile, 2-[2-hydroxy-3-[[2-(1H-indol-3-yl)-1,1-dimethylethyl]amino]propoxy]- (9CI) (CA INDEX NAME)



L44 ANSWER 15 OF 34 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 2002:428760 HCAPLUS
DN 137:24314
TI Methods and apparatus for determining and utilizing the viscosity of circulating blood over a range of shear rates for diagnostics and treatment
IN Kensey, Kenneth; Hokanson, Charles
PA Visco Technologies, Inc., USA; Rheologics, Inc.
SO PCT Int. Appl., 98 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 8

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002043806	A2	20020606	WO 2001-US44352	20011127
	WO 2002043806	A3	20030327		
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	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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	NZ 502905	A	20010831	NZ 1998-502905	19980826
	JP 2001514384	T2	20010911	JP 2000-507994	19980826
	NO 2000000944	A	20000225	NO 2000-944	20000225
	US 2002061835	A1	20020523	US 2001-828761	20010409
	US 2003078517	A1	20030424	US 2001-839785	20010420
	AU 2002026986	A5	20020611	AU 2002-26986	20011127
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	US 2000-727950	A	20001201		
	US 2001-819924	A	20010328		
	US 2001-828761	A	20010409		
	US 2001-839785	A	20010420		
	US 1997-919906	A	19970828		
	WO 1998-US17657	W	19980826		
	US 1999-439795	A2	19991112		
	US 2000-501856	A2	20000210		
	US 2000-628401	A2	20000801		
	WO 2001-US44352	W	20011127		

AB Various methods are provided for determining and utilizing the viscosity of the circulating blood of a living being over a range of shear rates for diagnostics and treatment, such as detecting/reducing blood viscosity, work of the heart, contractility of the heart, for detecting/reducing the surface tension of the blood, for detecting plasma viscosity, for explaining/countering endothelial cell dysfunction, for providing high and low blood vessel wall shear stress data, red blood cell deformability data, lubricity of blood, and for treating different ailments such as peripheral arterial disease in combination with administering to a living being at least one pharmaceutically acceptable agent. Agents pharmaceutically effective to regulate at least one of the aforementioned blood parameters are used to adjust distribution of a substance through the bloodstream.

IC ICM A61P009-00
ICS A61P007-00; A61K031-00

CC 63-6 (**Pharmaceuticals**)

IT Proteins
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(blood; methods and apparatus for determining and utilizing the viscosity of circulating blood over a range of shear rates for diagnostics and treatment)

IT Adrenoceptor antagonists
Antiarrhythmics
Anticholesteremic agents
Anticoagulants
Antidiabetic agents
Antihypertensives
Antiobesity agents
Appetite depressants
Calcium channel blockers
Circulation
Diuretics
Electrolytes
Hypolipemic agents
Platelet aggregation inhibitors
Vasodilators
(methods and apparatus for determining and utilizing the viscosity of circulating blood over a range of shear rates for diagnostics and treatment)

IT Clays, biological studies
Gelatins, biological studies
Polyoxyalkylenes, biological studies
RL: MOA (Modifier or additive use); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(methods and apparatus for determining and utilizing the viscosity of circulating blood over a range of shear rates for diagnostics and treatment)

IT Amino acids, biological studies
Antibodies and Immunoglobulins
Estrogens
Hemoglobins
Minerals, biological studies
Progestogens
Thrombomodulin
Vitamins
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(methods and apparatus for determining and utilizing the viscosity of circulating blood over a range of shear rates for diagnostics and treatment)

IT Albumins, biological studies
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(serum; methods and apparatus for determining and utilizing the viscosity of circulating blood over a range of shear rates for diagnostics and

treatment)

IT Bentonite, biological studies
RL: MOA (Modifier or additive use); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(sodian; methods and apparatus for determining and utilizing the viscosity of circulating blood over a range of shear rates for diagnostics and treatment)

IT 187741-48-6, CHF 1521
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(CHF 1521; methods and apparatus for determining and utilizing the viscosity of circulating blood over a range of shear rates for diagnostics and treatment)

IT 192939-46-1, H 376/95
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(H 376/95; methods and apparatus for determining and utilizing the viscosity of circulating blood over a range of shear rates for diagnostics and treatment)

IT 9041-08-1, OP 2000
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(OP 2000; methods and apparatus for determining and utilizing the viscosity of circulating blood over a range of shear rates for diagnostics and treatment)

IT 7631-86-9, Silica, biological studies 9000-69-5, Pectin 9002-18-0, Agar 9004-34-6, Cellulose, biological studies 9004-67-5, Methyl cellulose 25322-68-3, Peg
RL: MOA (Modifier or additive use); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(methods and apparatus for determining and utilizing the viscosity of circulating blood over a range of shear rates for diagnostics and treatment)

IT 50-28-2, Estradiol, biological studies 50-78-2, Aspirin 52-01-7, Spironolactone 52-53-9, Verapamil 54-11-5, Nicotine 54-31-9, Furosemide 55-63-0, Nitroglycerin 57-63-6, Ethinylestradiol 58-32-2, Dipyridamole 58-54-8, Ethacrynic acid 58-93-5, Hydrochlorothiazide 58-94-6, Chlorothiazide 59-66-5, Acetazolamide 68-22-4, Norethindrone 69-65-8, D-Mannitol 70-51-9 72-33-3, Mestranol 81-81-2, Warfarin 86-54-4, Hydralazine 87-33-2, Isosorbide dinitrate 94-20-2, Chlorpropamide 122-09-8, Phentermine 396-01-0, Triamterene 520-85-4, Medroxyprogesterone 525-66-6, Propranolol 634-03-7, Phendimetrazine 637-07-0, Clofibrate 657-24-9, Metformin 797-63-7, Levonorgestrel 1156-19-0, Tolazamide 1231-93-2, Ethynodiol 2098-66-0, Cyproterone 3056-17-5, Stavudine 3930-20-9, Sotalol 4291-63-8, Cladribine 6533-00-2, Norgestrel 8001-27-2, Hirudin 9000-94-6, Antithrombin 9002-01-1, Streptokinase 9002-72-6, Somatotropin 9004-10-8, Insulin, biological studies 9004-54-0, Dextran, biological studies 9005-27-0, Hetastarch 9007-12-9, Calcitonin 9039-53-6, Urokinase 10238-21-8, Glyburide 11041-12-6, Cholestyramine 12650-69-0, Mupirocin 13523-86-9, Pindolol 15291-77-7, Ginkgolide b 15307-86-5, Diclofenac 16051-77-7, Isosorbide mononitrate 17560-51-9, Metolazone 18559-94-9, Salbutamol 21256-18-8, Oxaprozin 21829-25-4, Nifedipine 25614-03-3, Bromocriptine 25812-30-0, Gemfibrozil 26807-65-8, Indapamide 26839-75-8, Timolol 28395-03-1, Bumetanide 28523-86-6, Sevoflurane 28721-07-5, Oxcarbazepine 29094-61-9, Glipizide 29122-68-7, Atenolol 29457-07-6, Ticarcillin disodium 30516-87-1, Zidovudine 32222-06-3, Calcitriol 34391-04-3, Levosalbutamol 34580-13-7, Ketotifen 34911-55-2, Bupropion 35189-28-7, Norgestimate 38304-91-5, Minoxidil 39562-70-4, Nitrendipine 42200-33-9, Nadolol 42399-41-7, Diltiazem 42924-53-8, Nabumetone 47141-42-4, Levobunolol 49562-28-9, Fenofibrate 50925-79-6, Colestipol 51384-51-1, Metoprolol 54024-22-5, Desogestrel 55142-85-3, Ticlopidine 55985-32-5, Nicardipine 56180-94-0, Acarbose 56211-40-6, Torsemide 56420-45-2, Epirubicin 59122-46-2, Misoprostol

60202-16-6, Blood-coagulation factor XIV 60282-87-3, Gestodene
62571-86-2, Captopril 63612-50-0, Nilutamide 63675-72-9, Nisoldipine
64221-86-9, Imipenem 64544-07-6, Cefuroxime axetil 64706-54-3,
Bepridil 66085-59-4, Nimodipine 66722-44-9, Bisoprolol 67227-56-9,
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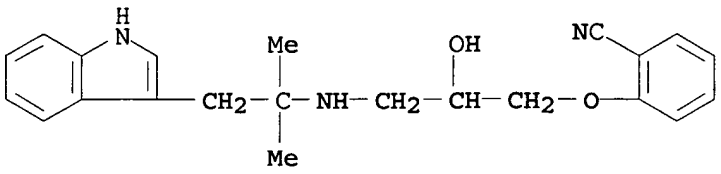
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(methods and apparatus for determining and utilizing the viscosity of circulating blood over a range of shear rates for diagnostics and treatment)

IT **71119-11-4**, Bucindolol
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)

(methods and apparatus for determining and utilizing the viscosity of circulating blood over a range of shear rates for diagnostics and treatment)

RN 71119-11-4 HCAPLUS

CN Benzonitrile, 2-[2-hydroxy-3-[[2-(1H-indol-3-yl)-1,1-dimethylethyl]amino]propoxy]- (9CI) (CA INDEX NAME)



L44 ANSWER 16 OF 34 HCAPLUS COPYRIGHT 2006 ACS on STN

AN 2002:420233 HCAPLUS

DN 138:32607

TI NPS-2143

AU Doggrell, Sheila A.; Del Fresno, M.; Castaner, J.

CS Department of Physiology and Pharmacology, School of Biomedical Sciences, University of Queensland, Brisbane, 4072, Australia

SO Drugs of the Future (2002), 27(2), 140-142
CODEN: DRFUD4; ISSN: 0377-8282

PB Prous Science

DT Journal; General Review

LA English

AB A review. Efforts to discover new treatments for **osteoporosis** led to the identification of the potent and selective, small-mol. **calcium** receptor antagonist NPS-2143. NPS-2143 is the prototype **calcilytic** drug, designed to act on **calcium** receptors on the surface of parathyroid glands, stimulating the release of the body's own stores of native parathyroid hormone (PTH). In **osteopenic** ovariectomized rats, daily oral administration of NPS-2143 resulted in moderate but sustained increases in plasma PTH levels and marked increases in **bone** formation and resorption, with no net **bone** gain or loss. The combination of NPS-2143 and estrogen increases **bone** formation and d. to a greater extent than either agent alone. These results suggest that NPS-2143 may be useful in the treatment of established **osteoporosis.**

CC 1-0 (Pharmacology)

ST review **calcium** receptor antagonist NPS 2143 **osteoporosis** estrogen

IT **Bone** formation
Bone resorption
Bone resorption inhibitors
Calcium channel blockers
Osteoporosis
(**calcium** antagonist NPS-2143: action mechanism in **osteoporosis** treatment)

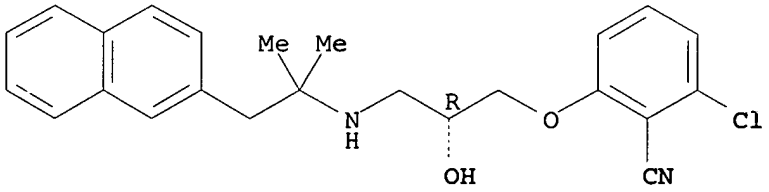
IT Parathyroid gland
(**calcium** receptors; **calcium** antagonist NPS-2143: action mechanism in **osteoporosis** treatment)

IT Receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**calcium**, parathyroid; **calcium** antagonist NPS-2143: action mechanism in **osteoporosis** treatment)

IT Estrogens
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL

(Biological study); USES (Uses)
(combination with NPS-2143; **calcium** antagonist NPS-2143: action mechanism in **osteoporosis** treatment)
IT Drug interactions
(synergistic; **calcium** antagonist NPS-2143: action mechanism in **osteoporosis** treatment)
IT 9002-64-6, Parathyroid hormone
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**calcium** antagonist NPS-2143: action mechanism in **osteoporosis** treatment)
IT **284035-33-2**, NPS-2143
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(**calcium** antagonist NPS-2143: action mechanism in **osteoporosis** treatment)
IT 50-28-2, 17β-Estradiol, biological studies
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(combination with NPS-2143; **calcium** antagonist NPS-2143: action mechanism in **osteoporosis** treatment)
IT **284035-33-2**, NPS-2143
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(**calcium** antagonist NPS-2143: action mechanism in **osteoporosis** treatment)
RN 284035-33-2 HCAPLUS
CN Benzonitrile, 2-chloro-6-[(2R)-3-[[1,1-dimethyl-2-(2-naphthalenyl)ethyl]amino]-2-hydroxypropoxy]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 17 OF 34 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 2002:392219 HCAPLUS
DN 136:406945
TI Methods for in vivo drug delivery based on monitoring blood flow parameters
IN Kensey, Kenneth R.
PA USA
SO U.S. Pat. Appl. Publ., 40 pp., Cont.-in-part of U.S. Ser. No. 727,950.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 8

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PI	US 2002061835	A1	20020523	US 2001-828761	20010409
	US 6019735	A	20000201	US 1997-919906	19970828
	CA 2301161	AA	19990304	CA 1998-2301161	19980826

NZ 502905	A	20010831	NZ 1998-502905	19980826
JP 2001514384	T2	20010911	JP 2000-507994	19980826
US 6322524	B1	20011127	US 1999-439795	19991112
US 6322525	B1	20011127	US 2000-501856	20000210
NO 2000000944	A	20000225	NO 2000-944	20000225
US 6428488	B1	20020806	US 2000-615340	20000712
WO 2002043806	A2	20020606	WO 2001-US44352	20011127
WO 2002043806	A3	20030327		
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AU 2002026986	A5	20020611	AU 2002-26986	20011127
US 2002088953	A1	20020711	US 2001-33841	20011227
US 6624435	B2	20030923		
WO 2002079778	A2	20021010	WO 2002-US3984	20020207
WO 2002079778	A3	20030710		
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2002184941	A1	20021212	US 2002-156165	20020528
US 6571608	B2	20030603		
PRAI US 1997-919906	A2	19970828		
US 1999-439795	A2	19991112		
US 2000-501856	A2	20000210		
US 2000-628401	A2	20000801		
US 2000-727950	A2	20001201		
US 1997-966076	A	19971107		
WO 1998-US17657	W	19980826		
US 2000-615340	A3	20000712		
US 2000-228612P	P	20000828		
US 2001-789350	B2	20010221		
US 2001-819924	A	20010328		
US 2001-828761	A	20010409		
US 2001-839785	A	20010420		
US 2001-841389	A	20010424		
US 2001-897164	A3	20010702		
WO 2001-US44352	W	20011127		

AB Various methods are provided for determining and utilizing the viscosity of the circulating blood of a living being over a range of shear rates for diagnostics and treatment, such as detecting/reducing blood viscosity, work of the heart, contractility of the heart, for detecting/reducing the surface tension of the blood, for detecting plasma viscosity, for explaining/countering endothelial cell dysfunction, for providing high and low blood vessel wall shear stress data, red blood cell deformability data, lubricity of blood, and for treating different ailments such as peripheral arterial disease in combination with administering to a living

being at least one pharmaceutically acceptable agent. Agents pharmaceutically effective to regulate at least one of the aforementioned blood parameters are used to adjust distribution of a substance through the bloodstream.

IC ICM A61K031-00
ICS A61B005-00

INCL 514001000

CC 63-8 (**Pharmaceuticals**)
Section cross-reference(s): 1

IT Proteins
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(blood; methods for in vivo drug delivery based on monitoring blood flow parameters)

IT Clays, biological studies
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(colloidal; methods for in vivo drug delivery based on monitoring blood flow parameters)

IT Biopolymers
Gelatins, biological studies
Polymers, biological studies
Polyoxyalkylenes, biological studies
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(gels; methods for in vivo drug delivery based on monitoring blood flow parameters)

IT Adrenoceptor antagonists
Agglutination
Antiarrhythmics
Anticholesteremic agents
Anticoagulants
Antidiabetic agents
Antihypertensives
Antiobesity agents
Appetite depressants
Blood coagulation
Calcium channel blockers
Cardiac contraction
Circulation
Drug delivery systems
Drug dependence
Electrolytes, biological
Human
Hypolipemic agents
Platelet aggregation
Platelet aggregation
Platelet aggregation inhibitors
Psychotropics
Surfactants
Thixotropy
Vasodilators
(methods for in vivo drug delivery based on monitoring blood flow parameters)

IT Amino acids, biological studies
Antibodies and Immunoglobulins
Estrogens
Hemoglobins
Mineral elements, biological studies
Progestogens
Thrombomodulin
Vitamins
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)

(methods for in vivo drug delivery based on monitoring blood flow parameters)

IT Albumins, biological studies
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(serum; methods for in vivo drug delivery based on monitoring blood flow parameters)

IT Bentonite, biological studies
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(sodian; methods for in vivo drug delivery based on monitoring blood flow parameters)

IT 7631-86-9, Colloidal silica, biological studies
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(colloidal; methods for in vivo drug delivery based on monitoring blood flow parameters)

IT 9000-69-5, Pectin 9002-18-0, Agar 9004-67-5, Methyl cellulose 25322-68-3, Polyethylene glycol
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(gels; methods for in vivo drug delivery based on monitoring blood flow parameters)

IT 50-28-2, Estradiol, biological studies 50-78-2, Aspirin 52-01-7, Spironolactone 52-53-9, Verapamil 54-11-5, Nicotine 54-31-9, Furosemide 55-63-0, Nitroglycerin 57-63-6, Ethinyl estradiol 58-32-2, Dipyridamole 58-54-8, Ethacrynic acid 58-93-5, Hydrochlorothiazide 58-94-6, Chlorothiazide 59-66-5, Acetazolamide 68-22-4, Norethindrone 69-65-8, D-Mannitol 70-51-9 72-33-3, Mestranol 81-81-2, Warfarin 86-54-4, Hydralazine 87-33-2, Isosorbide dinitrate 94-20-2, Chlorpropamide 122-09-8, Phentermine 396-01-0, Triamterene 520-85-4, Medroxyprogesterone 525-66-6, Propranolol 634-03-7, Phendimetrazine 637-07-0, Clofibrate 657-24-9, Metformin 797-63-7, Levonorgestrel 1156-19-0, Tolazamide 1231-93-2, Ethynodiol 2098-66-0, Cyproterone 3056-17-5, Stavudine 3930-20-9, Sotalol 4291-63-8, Cladribine 6533-00-2, Norgestrel 8001-27-2, Hirudin 9000-94-6, Antithrombin III 9002-01-1, Streptokinase 9002-72-6, Somatotropin 9004-10-8, Insulin, biological studies 9004-54-0, Dextran, biological studies 9005-27-0, Hetastarch 9007-12-9, Calcitonin 9039-53-6, Urokinase 9041-08-1, OP 2000 10238-21-8, Glyburide 11041-12-6, Cholestyramine 12650-69-0, Mupirocin 13523-86-9, Pindolol 15291-77-7, Ginkgolide B 15307-86-5, Diclofenac 16051-77-7, Isosorbide mononitrate 17560-51-9, Metolazone 18559-94-9, Salbutamol 21256-18-8, Oxaprozin 21829-25-4, Nifedipine 24967-94-0, Dermatan sulfate 25614-03-3, Bromocriptine 25812-30-0, Gemfibrozil 26807-65-8, Indapamide 26839-75-8, Timolol 28395-03-1, Bumetanide 28523-86-6, Sevoflurane 28721-07-5, Oxcarbazepine 29094-61-9, Glipizide 29122-68-7, Atenolol 29457-07-6, Ticarcillin disodium 30516-87-1, Zidovudine 32222-06-3, Calcitriol 34391-04-3, Levosalbutamol 34580-13-7, Ketotifen 34911-55-2, Bupropion 35189-28-7, Norgestimate 38304-91-5, Minoxidil 42200-33-9, Nadolol 42399-41-7, Diltiazem 42924-53-8, Nabumetone 47141-42-4, Levobunolol 49562-28-9, Fenofibrate 50925-79-6, Colestipol 51333-22-3, Budesonide 51384-51-1, Metoprolol 54024-22-5, Desogestrel 55142-85-3, Ticlopidine 55985-32-5, Nicardipine 56180-94-0, Acarbose 56211-40-6, Torsemide 56420-45-2, Epirubicin 59122-46-2, Misoprostol 60282-87-3, Gestodene 62571-86-2, Captopril 63612-50-0, Nilutamide 63675-72-9, Nisoldipine 64221-86-9, Imipenem 64544-07-6, Cefuroxime axetil 64706-54-3, Bepridil 66085-59-4, Nimodipine 66722-44-9, Bisoprolol 67227-56-9, Fenoldopam 68252-19-7, Pirmenol 68291-97-4, Zonisamide 69655-05-6, Didanosine **71119-11-4**, Bucindolol 71486-22-1, Vinorelbine 72509-76-3, Felodipine 72956-09-3, Carvedilol 73573-87-2, Formoterol 73963-72-1, Cilostazol 74191-85-8, Doxazosin 74863-84-6, Argatroban 75330-75-5, Lovastatin 75695-93-1, Isradipine 75847-73-3, Enalapril

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79350-37-1, Cefixime 79902-63-9, Simvastatin 80474-14-2, Fluticasone
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96829-58-2, Orlistat 97240-79-4, Topiramate 97322-87-7, Troglitazone
97682-44-5, Irinotecan 98048-97-6, Fosinopril 99522-79-9, Pranidipine
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Sematilide 102786-52-7, Blood-coagulation factor VII (human clone
λHVII2463 protein moiety) 103577-45-3, Lansoprazole
103745-39-7, Fasudil 103890-78-4, Lacidipine 104713-75-9, Barnidipine
105816-04-4, Nateglinide 105857-23-6, Alteplase 105979-17-7,
Benidipine 106650-56-0, Sibutramine 107452-89-1, Ziconotide
109889-09-0, Granisetron 111025-46-8, Pioglitazone 112809-51-5,
Letrozole 113665-84-2, Clopidogrel 113806-05-6, Olopatadine
114432-13-2, Fantofarone 114798-26-4, Losartan 114870-03-0,
Fondaparinux sodium 115103-54-3, Tiagabine 115256-11-6, Dofetilide
116308-55-5 117279-73-9, Israpafant 118457-14-0, Nebivolol
119684-05-8, Mesoglycan 120511-73-1, Anastrozole 120993-53-5,
Desirudin 121181-53-1, Filgrastim 121679-13-8, Naratriptan
122647-31-8, Ibutilide 123524-52-7, Azelnidipine 123774-72-1, Leukine
123948-87-8, Topotecan 124750-99-8, Losartan potassium 124832-26-4,
Valacyclovir 124937-51-5, Tolterodine 125670-52-2 128270-60-0,
Bivalirudin 128470-16-6, Arbutamine 129618-40-2, Nevirapine
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132579-32-9, Rocepafant 132875-61-7, Remifentanil 133040-01-4,
Eprosartan 133242-30-5, Landiolol 133652-38-7, Reteplase
134308-13-7, Tolcapone 134523-00-5, Atorvastatin 134678-17-4,
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138402-11-6, Irbesartan 138661-03-7, Furnidipine 143653-53-6,
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210101-16-9, Conivaptan 679809-58-6, Enoxaparin sodium
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(methods for in vivo drug delivery based on monitoring blood flow parameters)

IT 9004-34-6, Cellulose, biological studies
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(microcryst.; methods for in vivo drug delivery based on monitoring blood flow parameters)

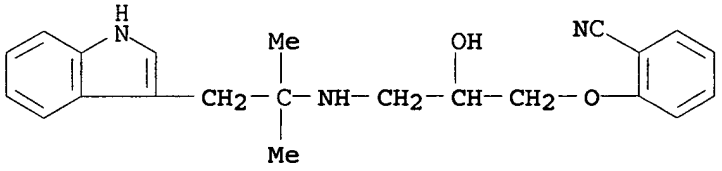
IT 12629-01-5, Somatropin
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(recombinant; methods for in vivo drug delivery based on monitoring blood flow parameters)

IT **71119-11-4**, Bucindolol
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)

(methods for in vivo drug delivery based on monitoring blood flow parameters)

RN 71119-11-4 HCAPLUS

CN Benzonitrile, 2-[2-hydroxy-3-[[2-(1H-indol-3-yl)-1,1-dimethylethyl]amino]propoxy]- (9CI) (CA INDEX NAME)



L44 ANSWER 18 OF 34 HCAPLUS COPYRIGHT 2006 ACS on STN

AN 2002:331982 HCAPLUS

DN 136:340584

TI Preparation of aryloxypropinolamine phosphate ester derivatives as antagonists of **calcium** receptor (**calcilytics**)

IN Bhatnagar, Pradip; Bryan, William M.; Callahan, James F.; Huffman, William F.

PA Smithkline Beecham Corporation, USA

SO PCT Int. Appl., 26 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002034204	A2	20020502	WO 2001-US46233	20011025
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	US 2004014723	A1	20040122	US 2003-415118	20030424
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OS MARPAT 136:340584

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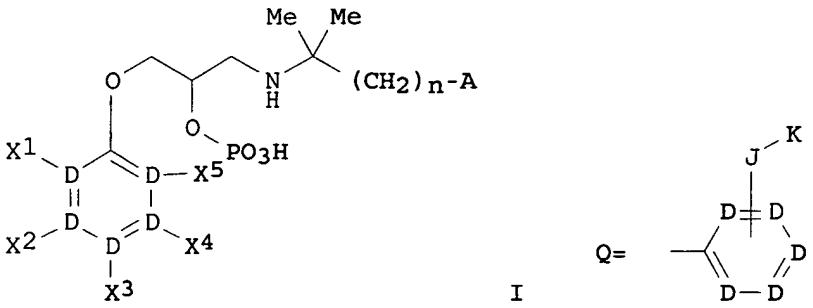


I

AB Novel **calcilytic** compds. [I; A = aryl or fused aryl, dihydro or tetrahydro fused aryl, heteroaryl or fused heteroaryl, dihydro or tetrahydro fused heteroaryl, unsubstituted or substituted with any substituent being selected from the group consisting of OH, halo, C1-4 alkyl, C1-4 alkoxy, C3-6 cycloalkyl, CF3, OCF3, cyano, and NO2; D is C or N with up to 2-N in ring, provided that X1-X5 are not present when D is N; X1 and X5 are independently selected from the group consisting of H, halo, cyano, and NO2, provided that either X1 or X5 is H; further provided that X1 and X5 are not present when D is N; X2 is selected from the group consisting of H, halo, C1-4 alkoxy, and J-K; X3 and X4 are selected from the group consisting of H, halo, C1-4 alkoxy, L, and J-K; J is a covalent bond, alkylene, O-alkylene or alkenylene; and K is selected from the group consisting of, CO2R5, CONR4R4', SO2NR4R4', OH, CHO, NR4R4', NR4SO2R4' and cyano; provided that X2, X3 and X4 are not present when D is N; L = Q; R4 and R4' are independently H, alkyl, aryl or heteroaryl; R5 is H, alkyl, alkyl-(O-alkyl)m-O-alkyl, aryl or heteroaryl; n is an integer from 0 to 4; m is an integer from 1 to 3], which are able to inhibit **calcium** receptor activity, thereby causing a decrease in one or more **calcium** receptor activities evoked by extracellular Ca2+ (no data), are prepared These compds. are useful for treating a disease or disorder characterized by an abnormal **bone** or mineral homeostasis which is selected from **osteosarcoma**, periodontal disease, fracture healing, **osteoarthritis**, joint replacement, rheumatoid arthritis, Paget's disease, humoral hypercalcemia, malignancy and **osteoporosis**. They are also used for increasing serum parathyroid levels. Thus, a solution of Et 4-[[3-[(R)-glycidyloxy]methyl-4-cyano]phenyl]benzoate (preparation given) and 2-(5-chlorothiophen-2-yl)-1,1-dimethylethylamine (preparation given) in dioxane/men was treated with LiClO4 and refluxed for 3 days to give 78.6% 3-[(R)-3-[2-(5-chlorothiophen-2-yl)-1,1-dimethylethylamino]-2-hydroxypropoxy]-4'-cyanobiphenyl-4-carboxylic acid Et ester which was allowed to stand in polyphosphoric acid at room temperature for 4 days to give 3-[(R)-3-[2-(5-chlorothiophen-2-yl)-1,1-dimethylethylamino]-2-(phosphonooxy)propoxy]-4'-cyanobiphenyl-4-carboxylic acid Et ester.

IC ICM A61K

CC 27-8 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1

ST aryloxypropinolamine phosphate ester prepn antagonist **calcium** receptor **calcilytic**; abnormal **bone** mineral homeostasis treatment aryloxypropinolamine phosphate ester prepn; **osteosarcoma** periodontal disease treatment aryloxypropinolamine phosphate ester prepn; **bone** fracture healing aryloxypropinolamine phosphate ester prepn; **osteoarthritis** joint replacement rheumatoid arthritis aryloxypropinolamine phosphate ester prepn; Paget disease aryloxypropinolamine phosphate ester prepn; humoral hypercalcemia

aryloxypropinolamine phosphate ester prepn; malignancy
osteoporosis aryloxypropinolamine phosphate ester prepn

IT **Bone**, disease
(Paget's; preparation of aryloxypropinolamine phosphate derivs. as antagonists of **calcium** receptor (**calcilytics**))

IT **Bone**, disease
(abnormality; preparation of aryloxypropinolamine phosphate derivs. as antagonists of **calcium** receptor (**calcilytics**))

IT Vitronectin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antagonists for, as anti-resorptive agents; preparation of aryloxypropinolamine phosphate derivs. as antagonists of **calcium** receptor (**calcilytics**))

IT Estrogens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(anti-resorptive agents; preparation of aryloxypropinolamine phosphate derivs. as antagonists of **calcium** receptor (**calcilytics**))

IT Receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**calcium**, antagonists for; preparation of aryloxypropinolamine phosphate derivs. as antagonists of **calcium** receptor (**calcilytics**))

IT **Bone**, disease
(fracture, healing; preparation of aryloxypropinolamine phosphate derivs. as antagonists of **calcium** receptor (**calcilytics**))

IT Estrogen receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(modulators for, as anti-resorptive agents; preparation of aryloxypropinolamine phosphate derivs. as antagonists of **calcium** receptor (**calcilytics**))

IT **Bone**, neoplasm
Sarcoma
(**osteosarcoma**; preparation of aryloxypropinolamine phosphate derivs. as antagonists of **calcium** receptor (**calcilytics**))

IT **Bone**, neoplasm
Homeostasis
Osteoarthritis
Osteoporosis
Periodontium, disease
Rheumatoid arthritis
(preparation of aryloxypropinolamine phosphate derivs. as antagonists of **calcium** receptor (**calcilytics**))

IT Parathyroid gland
(promoters for secretion of parathyroid hormone; preparation of aryloxypropinolamine phosphate derivs. as antagonists of **calcium** receptor (**calcilytics**))

IT Joint, anatomical
(replacement; preparation of aryloxypropinolamine phosphate derivs. as antagonists of **calcium** receptor (**calcilytics**))

IT Protein motifs
(src SH2 domain, antagonists for, as anti-resorptive agents; preparation of aryloxypropinolamine phosphate derivs. as antagonists of **calcium** receptor (**calcilytics**))

IT 9007-12-9, Calcitonin 32222-06-3, 1,25-Dihydroxyvitamin D3
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(anti-resorptive agent; preparation of aryloxypropinolamine phosphate derivs. as antagonists of **calcium** receptor (**calcilytics**))

IT 7440-70-2, **Calcium**, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(humoral hypercalcemia; preparation of aryloxypropinolamine phosphate derivs. as antagonists of **calcium** receptor (**calcilytics**))

IT 288067-35-6P, 2-Hydroxy-4-bromobenzonitrile 288067-36-7P, Ethyl 4-(3-hydroxy-4-cyanophenyl)benzoate 288067-37-8P 393813-65-5P, 2-(5-Chlorothiophen-2-yl)-1,1-dimethylethylamine 419565-60-9P, Ethyl 4-[3-[[(R)-glycidyloxy]methyl]-4-cyanophenyl]benzoate 419565-61-0P, 3-(5-Chlorothiophen-2-yl)-2,2-dimethylpropionic acid methyl ester 419565-62-1P, 3-(5-Chlorothiophen-2-yl)-2,2-dimethylpropionic acid 419565-63-2P, 2-Chloro-5-(2-isocyanato-2-methylpropyl)thiophene **419565-64-3P**, 3'-[[(R)-3-[[2-(5-Chlorothiophen-2-yl)-1,1-dimethylethyl]amino]-2-hydroxypropyl]oxy]-4'-cyanobiphenyl-4-carboxylic acid ethyl ester
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(intermediate; preparation of aryloxypropinolamine phosphate derivs. as antagonists of **calcium** receptor (**calcilytics**))

IT 34708-60-6P, Ethyl 3-hydroxybenzenepropionate 53273-37-3P, Indan-2-ylacetic acid methyl ester 246219-43-2P, Ethyl 4-cyano-3-hydroxybenzenepropionate 246219-46-5P, Ethyl (R)-4-cyano-3-(oxiranylmethoxy)benzenepropionate **351490-26-1P** 351490-85-2P, 2-Indan-2-yl-1,1-dimethylethylamine 351490-86-3P, 1-Indan-2-yl-2-methylpropan-2-ol 351490-87-4P, N-(2-Indan-2-yl-1,1-dimethylethyl)acetamide 351490-88-5P, Ethyl 4-formyl-3-hydroxybenzenepropionate 351490-89-6P, Ethyl 3-hydroxy-4-[(hydroxyimino)methyl]benzenepropionate 351490-90-9P, Ethyl 3-acetoxy-4-cyanobenzenepropionate
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(intermediate; preparation of aryloxypropinolamine phosphate ester derivs. as antagonists of **calcium** receptor (**calcilytics**) for treating disease or disorder characterized by abnormal **bone** or mineral homeostasis)

IT 419565-59-6P 419565-65-4P, 3'-[[(R)-3-[[2-(5-Chlorothiophen-2-yl)-1,1-dimethylethyl]amino]-2-phosphonooxypropyl]oxy]-4'-cyanobiphenyl-4-carboxylic acid ethyl ester 419565-66-5P, 3'-[[(R)-3-[[2-(5-Chlorothiophen-2-yl)-1,1-dimethylethyl]amino]-2-phosphonooxypropyl]oxy]-4'-cyanobiphenyl-4-carboxylic acid
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of aryloxypropinolamine phosphate derivs. as antagonists of **calcium** receptor (**calcilytics**))

IT 419565-58-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of aryloxypropinolamine phosphate ester derivs. as antagonists of **calcium** receptor (**calcilytics**) for treating disease or disorder characterized by abnormal **bone** or mineral homeostasis)

IT 9024-82-2, Pyrophosphatase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(proton-pumping, vacuolar proton ATPase, inhibitors for, as anti-resorptive agents; preparation of aryloxypropinolamine phosphate derivs. as antagonists of **calcium** receptor (**calcilytics**))

IT 547-63-7, Methyl isobutyrate 14047-29-1, p-Carboxybenzeneboronic acid

23784-96-5, 5-Chloro-2-chloromethylthiophene 179897-89-3, 2-Fluoro-5-bromobenzonitrile
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; preparation of aryloxypropinolamine phosphate derivs. as antagonists of **calcium** receptor (**calcilytics**))

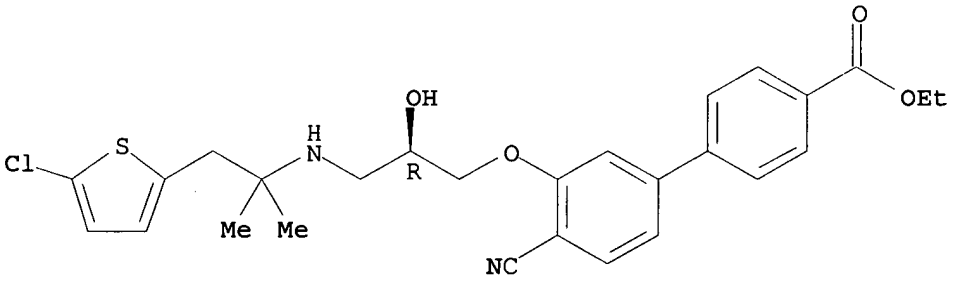
IT 621-54-5, 3-(3-Hydroxyphenyl)propionic acid 37868-26-1, Indan-2-ylacetic acid 115314-17-5, (2R)-Glycidyl 3-nitrobenzenesulfonate
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; preparation of aryloxypropinolamine phosphate ester derivs. as antagonists of **calcium** receptor (**calcilytics**) for treating disease or disorder characterized by abnormal **bone** or mineral homeostasis)

IT **419565-64-3P**, 3'-[[(R)-3-[[2-(5-Chlorothiophen-2-yl)-1,1-dimethylethyl]amino]-2-hydroxypropyl]oxy]-4'-cyanobiphenyl-4-carboxylic acid ethyl ester
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(intermediate; preparation of aryloxypropinolamine phosphate derivs. as antagonists of **calcium** receptor (**calcilytics**))

RN 419565-64-3 HCAPLUS

CN [1,1'-Biphenyl]-4-carboxylic acid, 3'-[(2R)-3-[[2-(5-chloro-2-thienyl)-1,1-dimethylethyl]amino]-2-hydroxypropoxy]-4'-cyano-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L44 ANSWER 19 OF 34 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 2002:185688 HCAPLUS
DN 136:252567
TI Methods for drug administration and distribution based on monitoring blood viscosity and other parameters for diagnostics and treatment
IN Kensey, Kenneth
PA USA
SO U.S. Pat. Appl. Publ., 46 pp., Cont.-in-part of U.S. Ser. No. 819,924.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 8

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002032149	A1	20020314	US 2001-841389	20010424
	US 6019735	A	20000201	US 1997-919906	19970828
	CA 2301161	AA	19990304	CA 1998-2301161	19980826
	NZ 502905	A	20010831	NZ 1998-502905	19980826
	JP 2001514384	T2	20010911	JP 2000-507994	19980826
	US 6322524	B1	20011127	US 1999-439795	19991112
	US 6322525	B1	20011127	US 2000-501856	20000210

NO	2000000944	A	20000225	NO 2000-944	20000225
US	6428488	B1	20020806	US 2000-615340	20000712
US	2002088953	A1	20020711	US 2001-33841	20011227
US	6624435	B2	20030923		
WO	2002079778	A2	20021010	WO 2002-US3984	20020207
WO	2002079778	A3	20030710		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US	2002184941	A1	20021212	US 2002-156165	20020528
US	6571608	B2	20030603		

PRAI	US 1997-919906	A2	19970828
	US 1999-439795	A2	19991112
	US 2000-501856	A2	20000210
	US 2000-628401	A2	20000801
	US 2000-727950	A2	20001201
	US 2001-819924	A2	20010328
	US 1997-966076	A	19971107
	WO 1998-US17657	W	19980826
	US 2000-615340	A3	20000712
	US 2000-228612P	P	20000828
	US 2001-789350	B2	20010221
	US 2001-828761	A	20010409
	US 2001-839785	A	20010420
	US 2001-841389	A	20010424
	US 2001-897164	A3	20010702

AB Various methods are provided for determining and utilizing the viscosity of the circulating blood of a living being, i.e., a human, over a range of shear rates for diagnostics and treatment, such as detecting/reducing blood viscosity, work of the heart, contractility of the heart, for detecting/reducing the surface tension of the blood, for detecting plasma viscosity, for explaining/countering endothelial cell dysfunction, for providing high and low blood vessel wall shear stress data, red blood cell deformability data, lubricity of blood, and for treating different ailments such as peripheral arterial disease in combination with administering to a living being at least one pharmaceutically acceptable agent. Agents pharmaceutically effective to regulate at least one of the aforementioned blood parameters are used to adjust distribution of a substance through the bloodstream. For example, when blood viscosity is a blood flow parameter monitored, an agent is selected from i.v. diluents, red blood cell deformability agents, antiurea agents, oral contraceptives, antidiabetic agents, antiarrhythmics, antihypertensives, antihyperlipidemics, antiplatelet agents, appetite suppressants, antiobesity agents, blood modifiers, smoking deterrent agents, and nutritional supplements.

IC ICM A61K031-00
ICS A61B005-00

INCL 514001000

CC 63-8 (**Pharmaceuticals**)
Section cross-reference(s): 1, 14

IT Adrenoceptor antagonists
Agglutination
Antiarrhythmics

Anticholesteremic agents
Anticoagulants
Antidiabetic agents
Antihypertensives
Antiobesity agents
Appetite depressants
Blood analysis
Blood coagulation
Calcium channel blockers
Cardiac contraction
Circulation
Diagnosis
Drug delivery systems
Drug delivery systems
Drug dependence
Electrolytes, biological
Human
Hypolipemic agents
Platelet aggregation
Platelet aggregation
Platelet aggregation inhibitors
Sedimentation (separation)
Surfactants
Therapy
Thixotropy
Tobacco products
Vasodilators
(apparatus and methods for monitoring blood viscosity and other parameters in drug delivery for diagnostics and treatment)

IT Amino acids, biological studies
Antibodies and Immunoglobulins
Estrogens
Gelatins, biological studies
Hemoglobins
Mineral elements, biological studies
Polyoxyalkylenes, biological studies
Progestogens
Thrombomodulin
Vitamins
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(apparatus and methods for monitoring blood viscosity and other parameters in drug delivery for diagnostics and treatment)

IT Proteins
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(blood; apparatus and methods for monitoring blood viscosity and other parameters in drug delivery for diagnostics and treatment)

IT Clays, biological studies
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(colloidal; apparatus and methods for monitoring blood viscosity and other parameters in drug delivery for diagnostics and treatment)

IT Biopolymers
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(gels; apparatus and methods for monitoring blood viscosity and other parameters in drug delivery for diagnostics and treatment)

IT Albumins, biological studies
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(serum; apparatus and methods for monitoring blood viscosity and other parameters in drug delivery for diagnostics and treatment)

IT Bentonite, biological studies
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)

(sodian, magma; apparatus and methods for monitoring blood viscosity and other parameters in drug delivery for diagnostics and treatment)

IT Magma
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(sodium bentonite; apparatus and methods for monitoring blood viscosity and other parameters in drug delivery for diagnostics and treatment)

IT 187741-48-6, CHF 1521
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(CHF 1521; apparatus and methods for monitoring blood viscosity and other parameters in drug delivery for diagnostics and treatment)

IT 50-28-2, Estradiol, biological studies 50-78-2, Aspirin 52-01-7, Spironolactone 52-53-9, Verapamil 54-11-5, Nicotine 54-31-9, Furosemide 55-63-0, Nitroglycerin 57-63-6, Ethinyl estradiol 58-32-2, Dipyridamole 58-54-8, Ethacrynic acid 58-93-5, Hydrochlorothiazide 58-94-6, Chlorothiazide 59-66-5, Acetazolamide 68-22-4, Norethindrone 69-65-8, Mannitol 70-51-9 72-33-3, Mestranol 81-81-2, Warfarin 86-54-4, Hydralazine 87-33-2, Isosorbide dinitrate 94-20-2, Chlorpropamide 122-09-8, Phentermine 396-01-0, Triamterene 520-85-4, Medroxyprogesterone 525-66-6, Propranolol 634-03-7, Phendimetrazine 637-07-0, Clofibrate 657-24-9, Metformin 797-63-7, Levonorgestrel 1156-19-0, Tolazamide 1231-93-2, Ethynodiol 2098-66-0, Cyproterone 3056-17-5, Stavudine 3930-20-9, Sotalol 4291-63-8, Cladribine 6533-00-2, Norgestrel 8001-27-2, Hirudin 9000-69-5, Pectin 9000-94-6, Antithrombin III 9002-01-1, Streptokinase 9002-18-0, Agar 9002-72-6, Somatotropin 9004-10-8, Insulin, biological studies 9004-54-0, Dextran, biological studies 9004-67-5, Methyl cellulose 9005-27-0, Hetastarch 9007-12-9, Calcitonin 9039-53-6, Urokinase 9041-08-1, OP 2000 10238-21-8, Glyburide 11041-12-6, Cholestyramine 12650-69-0, Mupirocin 13523-86-9, Pindolol 15291-77-7, Ginkgolide B 15307-86-5, Diclofenac 16051-77-7, Isosorbide mononitrate 17560-51-9, Metolazone 18559-94-9, Salbutamol 21256-18-8, Oxaprozin 21829-25-4, Nifedipine 24967-94-0, Dermatan sulfate 25322-68-3, Polyethylene glycol 25614-03-3, Bromocriptine 25812-30-0, Gemfibrozil 26807-65-8, Indapamide 26839-75-8, Timolol 28395-03-1, Bumetanide 28523-86-6, Sevoflurane 28721-07-5, Oxcarbazepine 29094-61-9, Glipizide 29122-68-7, Atenolol 29457-07-6, Ticarcillin disodium 30516-87-1, Zidovudine 32222-06-3, Calcitriol 34391-04-3, Levosalbutamol 34580-13-7, Ketotifen 34911-55-2, Bupropion 35189-28-7, Norgestimate 38304-91-5, Minoxidil 39562-70-4, Nitrendipine 42200-33-9, Nadolol 42399-41-7, Diltiazem 42924-53-8, Nabumetone 47141-42-4, Levobunolol 49562-28-9, Fenofibrate 50925-79-6, Colestipol 51333-22-3, Budesonide 51384-51-1, Metoprolol 54024-22-5, Desogestrel 55142-85-3, Ticlopidine 55985-32-5, Nicardipine 56180-94-0, Acarbose 56211-40-6, Torsemide 56420-45-2, Epirubicin 59122-46-2, Misoprostol 60202-16-6, Blood-coagulation factor XIV 60282-87-3, Gestodene 62571-86-2, Captopril 63612-50-0, Nilutamide 63675-72-9, Nisoldipine 64221-86-9, Imipenem 64544-07-6, Cefuroxime axetil 64706-54-3, Bepridil 66085-59-4, Nimodipine 66722-44-9, Bisoprolol 67227-56-9, Fenoldopam 68252-19-7, Pirmenol 68291-97-4, Zonisamide 69655-05-6, Didanosine **71119-11-4**, Bucindolol 71486-22-1, Vinorelbine 72509-76-3, Felodipine 72956-09-3, Carvedilol 73573-87-2, Formoterol 73963-72-1, Cilostazol 74191-85-8, Doxazosin 74863-84-6, Argatroban 75330-75-5, Lovastatin 75695-93-1, Isradipine 75847-73-3, Enalapril 76547-98-3, Lisinopril 77191-36-7, Nefiracetam 78415-72-2, Milrinone 79350-37-1, Cefixime 79902-63-9, Simvastatin 80474-14-2, Fluticasone propionate 81732-65-2, Bambuterol 82410-32-0, Ganciclovir 82834-16-0, Perindopril 83869-56-1, Granulocyte-macrophage colony-stimulating factor 84057-84-1, Lamotrigine 84057-95-4, Ropivacaine 84449-90-1, Raloxifene 84625-59-2, Dotarizine 85441-61-8, Quinapril 86541-75-5, Benazepril 86780-90-7, Aranidipine 87239-81-4, Cefpodoxime proxetil 87333-19-5,

Ramipril 87679-37-6, Trandolapril 88150-42-9, Amlodipine 89565-68-4, Tropisetron 90729-41-2, Oxodipine 91161-71-6, Terbinafine 92665-29-7, Cefprozil 93221-48-8, Levobetaxolol 93479-97-1, Glimepiride 93957-54-1, Fluvastatin 94535-50-9, Lemakalim 94739-29-4, Lemildipine 95058-81-4, Gemcitabine 96036-03-2, Meropenem 96125-53-0, Clentiazem 96829-58-2, Orlistat 97240-79-4, Topiramate 97322-87-7, Troglitazone 97682-44-5, Irinotecan 98048-97-6, Fosinopril 99522-79-9, Pranidipine 100427-26-7, Lercanidipine 100986-85-4, Levofloxacin 101526-83-4, Sematilide 102786-61-8, Blood-coagulation factor VIIa (human clone λHVII2463 protein moiety) 103577-45-3, Lansoprazole 103628-46-2, Sumatriptan 103745-39-7, Fasudil 103890-78-4, Lacidipine 104713-75-9, Barnidipine 105816-04-4, Nateglinide 105857-23-6, Alteplase 105979-17-7, Benidipine 106650-56-0, Sibutramine 107452-89-1, Ziconotide 109889-09-0, Granisetron 111025-46-8, Pioglitazone 112809-51-5, Letrozole 113665-84-2, Clopidogrel 113806-05-6, Olopatadine 114432-13-2, Fantofarone 114798-26-4, Losartan 114870-03-0, Fondaparinux sodium 115103-54-3, Tiagabine 115256-11-6, Dofetilide 116308-55-5, Watanidipine 117279-73-9, Israpafant 118457-14-0, Nebivolol 119684-05-8, Mesoglycan 120511-73-1, Anastrozole 120993-53-5, Desirudin 121181-53-1, Filgrastim 121679-13-8, Naratriptan 122647-31-8, Ibutilide 123524-52-7, Azelnidipine 123774-72-1, Sargramostim 123948-87-8, Topotecan 124750-99-8, Losartan potassium 124832-26-4, Valacyclovir 124937-51-5, Tolterodine 128270-60-0, Bivalirudin 128470-16-6, Arbutamine 129618-40-2, Nevirapine 130209-82-4, Latanoprost 130636-43-0, Nifekalant 131179-95-8, RSR 13 132579-32-9, Rocepafant 132875-61-7, Remifentanil 133040-01-4, Eprosartan 133242-30-5, Landiolol 133652-38-7, Reteplase 134308-13-7, Tolcapone 134523-00-5, Atorvastatin 134678-17-4, Lamivudine 134865-37-5, Meluadrine tartrate 135062-02-1, Repaglinide 136468-36-5, Foropafant 137862-53-4, Valsartan 138068-37-8, Lepirudin 138402-11-6, Irbesartan 138661-03-7, Furnidipine 143653-53-6, Abciximab 144494-65-5, Tirofiban 144689-63-4, Olmesartan medoxomil 144701-48-4, Telmisartan 145040-37-5, Candesartan cilexetil 145375-43-5, Mitiglinide 145599-86-6, Cerivastatin 147059-72-1, Trovafloxacin 147511-69-1, Pitavastatin 148883-56-1, Tifacogin 149908-53-2, Azimilide 150332-35-7, Pamaqueside 154189-24-9, ARC68397AA 158876-82-5, Rupatadine 159776-70-2, Melagatran 170902-47-3, Roxifiban 173324-94-2, Temiverine 187523-35-9, BMS204352
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(apparatus and methods for monitoring blood viscosity and other parameters in drug delivery for diagnostics and treatment)

IT 188627-80-7, Eptifibatide 210101-16-9, Conivaptan 679809-58-6, Enoxaparin sodium
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(apparatus and methods for monitoring blood viscosity and other parameters in drug delivery for diagnostics and treatment)

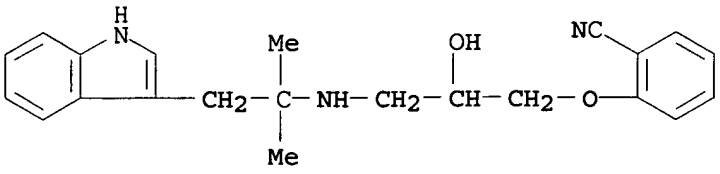
IT 7631-86-9, Colloidal silica, biological studies
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(colloidal; apparatus and methods for monitoring blood viscosity and other parameters in drug delivery for diagnostics and treatment)

IT 9004-34-6, Cellulose, biological studies
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(microcryst.; apparatus and methods for monitoring blood viscosity and other parameters in drug delivery for diagnostics and treatment)

IT **71119-11-4**, Bucindolol
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(apparatus and methods for monitoring blood viscosity and other parameters in drug delivery for diagnostics and treatment)

RN 71119-11-4 HCAPLUS

CN Benzonitrile, 2-[2-hydroxy-3-[[2-(1H-indol-3-yl)-1,1-dimethylethyl]amino]propoxy]- (9CI) (CA INDEX NAME)



L44 ANSWER 20 OF 34 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 2002:89783 HCAPLUS
DN 136:151076
TI Preparation of hydroxyphenoxypropylheteroarylethylamines, methoxyphenylethylaminophenoxypropanols, and related compounds as **calcilytic** compounds
IN Bhatnagar, Pradip K.; Callahan, James F.; Lago, Amparo M.
PA Smithkline Beecham Corporation, USA
SO PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002007673	A2	20020131	WO 2001-US22267	20010716
	WO 2002007673	A3	20031016		
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	AU 2001076923	A5	20020205	AU 2001-76923	20010716
	BR 2001012600	A	20030624	BR 2001-12600	20010716
	EP 1368318	A2	20031210	EP 2001-954696	20010716
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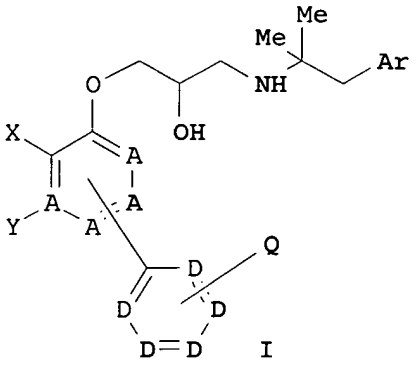
	JP 2004509077	T2	20040325	JP 2002-513411	20010716
	US 2003212110	A1	20031113	US 2003-333096	20030115
	US 6864267	B2	20050308		
	NO 2003000303	A	20030320	NO 2003-303	20030120
PRAI	US 2000-219842P	P	20000721		
	US 2000-220636P	P	20000725		
	WO 2001-US22267	W	20010716		

OS MARPAT 136:151076
GI



AB The preparation of **calcilytic** compds. [I; wherein A = C or N with one or two N's in ring; D = C or N with one or two N's in ring; X = CN, NO2, Cl, F, H; Y (when A = C) = H, halo; Q (when D = C) = H, alkyl, tetrazole, alc., etc.; Ar = Ph, naphthyl, heteroaryl, etc.] is described. Thus, a multistep synthesis of N-[(2R)-Hydroxy-3-[[2-cyano-5-[(5-carboxy)-3-pyridyl]phenoxy]propyl]]-1,1-dimethyl-2-(5-chlorothienyl)ethylamine is given. The prepared compds. are useful in the treatment of diseases or disorders characterized by an abnormal **bone** or mineral homeostasis, wherein the **bone** or mineral disease or disorder is selected from the group consisting of **osteosarcoma**, periodontal disease, fracture healing, **osteoarthritis**, joint replacement, rheumatoid arthritis, Paget's disease, humoral hypercalcemia associated with malignancy and fracture healing, and **osteoporosis.**

IC ICM A61K

CC 27-16 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1, **63**

ST **calcium** channel blocker prepn hydroxyphenoxypropylheteroarylethy lamine methoxyphenylethylaminophenoxypropanol; **calcilytic** compd prepn hydroxyphenoxypropylheteroarylethylamine methoxyphenylethylaminophenoxypropanol; mineral **bone** disease treatment prepn hydroxyphenoxypropylheteroarylethylamine methoxyphenylethylaminophenoxypropanol

IT **Bone**, disease
(Paget's, treatments; preparation of hydroxyphenoxypropylheteroarylethylamin es, methoxyphenylethylaminophenoxypropanols, and related compds. as **calcilytic** compds.)

IT Protein motifs
(SH2 domain, co-administration with src SH2 antagonists; preparation of hydroxyphenoxypropylheteroarylethylamines, methoxyphenylethylaminophenoxypropanols, and related compds. as **calcilytic** compds.)

IT Receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**calcium**, antagonists; preparation of hydroxyphenoxypropylheteroarylethylamines, methoxyphenylethylaminophenoxypropanols, and related compds. as **calcilytic** compds.)

IT Vitronectin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(co-administration with antagonists; preparation of hydroxyphenoxypropylheteroarylethylamines, methoxyphenylethylaminophenoxypropanols, and related compds. as **calcilytic** compds.)

IT Estrogen receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(co-administration with selective modulators; preparation of hydroxyphenoxypropylheteroarylethylamines, methoxyphenylethylaminophenoxypropanols, and related compds. as **calcilytic** compds.)

IT Estrogens
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(co-administration with; preparation of hydroxyphenoxypropylheteroarylethylamines, methoxyphenylethylaminophenoxypropanols, and related compds. as **calcilytic** compds.)

IT **Bone**, disease
(fracture, treatment; preparation of hydroxyphenoxypropylheteroarylethylamines, methoxyphenylethylaminophenoxypropanols, and related compds. as **calcilytic** compds.)

IT Neoplasm
(humoral hypercalcemia of malignancy, treatment; preparation of hydroxyphenoxypropylheteroarylethylamines, methoxyphenylethylaminophenoxypropanols, and related compds. as **calcilytic** compds.)

IT **Bone** resorption
(inhibitors; preparation of hydroxyphenoxypropylheteroarylethylamines, methoxyphenylethylaminophenoxypropanols, and related compds. as **calcilytic** compds.)

IT **Bone**, neoplasm
(**osteosarcoma**, inhibitors; preparation of hydroxyphenoxypropylheteroarylethylamines, methoxyphenylethylaminophenoxypropanols, and related compds. as **calcilytic** compds.)

IT **Bone**, neoplasm
Sarcoma
(**osteosarcoma**, treatment; preparation of hydroxyphenoxypropylheteroarylethylamines, methoxyphenylethylaminophenoxypropanols, and related compds. as **calcilytic** compds.)

IT Antitumor agents
(**osteosarcoma**; preparation of hydroxyphenoxypropylheteroarylethylamines, methoxyphenylethylaminophenoxypropanols, and related compds. as **calcilytic** compds.)

IT Antiarthritics
Antirheumatic agents
Calcium channel blockers
(preparation of hydroxyphenoxypropylheteroarylethylamines, methoxyphenylethylaminophenoxypropanols, and related compds. as **calcilytic** compds.)

IT **Osteoporosis**
(therapeutic agents; preparation of hydroxyphenoxypropylheteroarylethylamines, methoxyphenylethylaminophenoxypropanols, and related compds. as **calcilytic** compds.)

IT Homeostasis
(treatment of disorders of abnormal **bone** or mineral homeostasis; preparation of hydroxyphenoxypropylheteroarylethylamines, methoxyphenylethylaminophenoxypropanols, and related compds. as **calcilytic** compds.)

IT Periodontium, disease
(treatment; preparation of hydroxyphenoxypropylheteroarylethylamines, methoxyphenylethylaminophenoxypropanols, and related compds. as **calcilytic** compds.)

IT 94716-09-3, Cathepsin K
RL: BSU (Biological study, unclassified); BIOL (Biological study)

(co-administration with inhibitors of; preparation of hydroxyphenoxypropylheteroarylethylamines, methoxyphenylethylaminophenoxypropanols, and related compds. as **calcilytic** compds.)

IT 9007-12-9, Calcitonin
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(co-administration with; preparation of hydroxyphenoxypropylheteroarylethylamines, methoxyphenylethylaminophenoxypropanols, and related compds. as **calcilytic** compds.)

IT 7440-70-2, **Calcium**, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(humoral hypercalcemia of malignancy, treatment; preparation of hydroxyphenoxypropylheteroarylethylamines, methoxyphenylethylaminophenoxypropanols, and related compds. as **calcilytic** compds.)

IT **393813-39-3P 393813-41-7P 393813-43-9P**
393813-45-1P 393813-47-3P 393813-49-5P
393813-51-9P 393813-53-1P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); **PREP (Preparation)**; RACT (Reactant or reagent); USES (Uses)
(preparation of hydroxyphenoxypropylheteroarylethylamines, methoxyphenylethylaminophenoxypropanols, and related compds. as **calcilytic** compds.)

IT **393813-40-6P 393813-42-8P 393813-44-0P**
393813-46-2P 393813-48-4P 393813-50-8P
393813-52-0P 393813-54-2P 393813-55-3P 393813-56-4P
393813-66-6P 393813-67-7P 395109-48-5P
395109-49-6P 395109-51-0P 395109-53-2P
395109-55-4P 395109-56-5P 395109-58-7P 395109-60-1P
395109-61-2P 395109-63-4P 395109-64-5P 395109-65-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation of hydroxyphenoxypropylheteroarylethylamines, methoxyphenylethylaminophenoxypropanols, and related compds. as **calcilytic** compds.)

IT 74-88-4, Methyl iodide, reactions 6602-32-0, 2-Bromo-3-hydroxypyridine 14047-29-1, 4-Carboxyphenylboronic acid 15366-62-8, 4-Bromonicotinic acid 21190-87-4, 6-Bromopicolinic acid 56490-94-9 105942-08-3, 4-Bromo-2-fluorobenzonitrile 115314-17-5 351490-85-2 393813-65-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of hydroxyphenoxypropylheteroarylethylamines, methoxyphenylethylaminophenoxypropanols, and related compds. as **calcilytic** compds.)

IT 24059-89-0P 24100-18-3P, 2-Bromo-3-methoxypyridine 393813-57-5P
393813-58-6P 393813-59-7P 393813-60-0P 393813-61-1P 393813-62-2P
393813-63-3P 393813-64-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of hydroxyphenoxypropylheteroarylethylamines, methoxyphenylethylaminophenoxypropanols, and related compds. as **calcilytic** compds.)

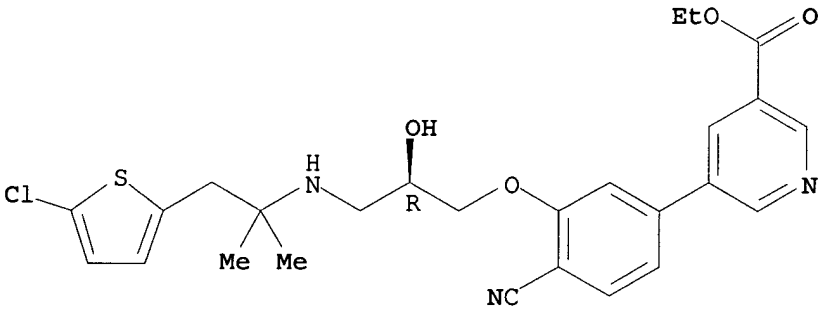
IT 13598-36-2D, Phosphonic acid, alkylidenebis- derivs. 32222-06-3
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(preparation of hydroxyphenoxypropylheteroarylethylamines, methoxyphenylethylaminophenoxypropanols, and related compds. as **calcilytic** compds.)

IT **393813-39-3P**
RL: PAC (Pharmacological activity); RCT (Reactant); **THU (Therapeutic**

use); THU (Therapeutic use); PREP (Preparation);
PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of hydroxyphenoxypropylheteroarylethylamines, methoxyphenylethylaminophenoxypropanols, and related compds. as **calcilytic** compds.)

RN 393813-39-3 HCAPLUS
CN 3-Pyridinecarboxylic acid, 5-[3-[(2R)-3-[[2-(5-chloro-2-thienyl)-1,1-dimethylethyl]amino]-2-hydroxypropoxy]-4-cyanophenyl]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L44 ANSWER 21 OF 34 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 2002:71857 HCAPLUS
DN 136:139826
TI Selective cyclooxygenase-2 inhibitors and vasomodulator compounds for generalized pain and headache pain
IN Hassan, Fred; Forbes, James C.
PA Pharmacia Corporation, USA
SO PCT Int. Appl., 218 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002005799	A2	20020124	WO 2001-US22103	20010713
	WO 2002005799	A3	20021121		
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	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2415697	AA	20020124	CA 2001-2415697	20010713
	AU 2001082886	A5	20020130	AU 2001-82886	20010713
	US 2002077328	A1	20020620	US 2001-905292	20010713
	EP 1299122	A2	20030409	EP 2001-961637	20010713
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP 2004503588	T2	20040205	JP 2002-511732	20010713
PRAI	US 2000-218101P	P	20000713		
	US 2001-284248P	P	20010417		

US 2001-296196P P 20010606
WO 2001-US22103 W 20010713
OS MARPAT 136:139826
AB A therapeutic combination useful in the treatment, amelioration, prevention, or delay of pain comprising a high energy form of a selective cyclooxygenase-2 inhibitor, a vasomodulator, and a pharmaceutically acceptable excipient, carrier, or diluent, the cyclooxygenase-2 inhibitor and vasomodulator each being present in an amount effective to contribute to the treatment, prevention, or delay of pain. Thus, capsules contained celecoxib 200, Labrasol 280, diethylene glycol monoethyl ether 280, and propylene glycol laurate 140/capsule.
IC ICM A61K031-00
CC 63-6 (**Pharmaceuticals**)
Section cross-reference(s): 1
IT Adrenoceptor agonists
Adrenoceptor antagonists
Analgesics
Antimigraine agents
Calcium channel blockers
Digestive tract
Drug bioavailability
Drug delivery systems
Human
Lubricants
Particle size distribution
Solvents
Vasodilators
(cyclooxygenase-2 inhibitors and vasomodulators for generalized pain and headache pain treatment)
IT Glycols, biological studies
Polyoxyalkylenes, biological studies
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(cyclooxygenase-2 inhibitors and vasomodulators for generalized pain and headache pain treatment)
IT Glycols, biological studies
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(ethers; cyclooxygenase-2 inhibitors and vasomodulators for generalized pain and headache pain treatment)
IT Ethers, biological studies
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(glycol; cyclooxygenase-2 inhibitors and vasomodulators for generalized pain and headache pain treatment)
IT 169590-42-5, Celecoxib
RL: PKT (Pharmacokinetics); PRP (Properties); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(cyclooxygenase-2 inhibitors and vasomodulators for generalized pain and headache pain treatment)
IT 50-60-2, Phentolamine 51-61-6, Dopamine, biological studies 55-63-0, Nitroglycerin 58-08-2, Caffeine, biological studies 58-55-9, Theophylline, biological studies 69-89-6, Xanthine 69-89-6D, Xanthine, derivs. 83-67-0, Theobromine 86-54-4, Hydralazine 87-33-2, Isosorbide dinitrate 111-90-0, Diethylene glycol monoethyl ether 364-98-7, Diazoxide 15078-28-1, Nitroprusside 19216-56-9, Prazosin 21829-25-4, Nifedipine 25322-68-3, Polyethylene glycol 34368-04-2, Dobutamine 36894-69-6, Labetalol 38304-91-5, Minoxidil 60719-84-8, Amrinone 62571-86-2, Captopril 65141-46-0, Nicorandil **71119-11-4**, Bucindolol 71125-38-7, Meloxicam 72509-76-3, Felodipine 72956-09-3, Carvedilol 75847-73-3, Enalapril 76420-72-9, Enalaprilat 76547-98-3, Lisinopril 78415-72-2, Milrinone 78794-60-2 81840-15-5, Vesnarinone 85441-61-8, Quinapril 87333-19-5, Ramipril

88150-42-9, Amlodipine 114798-26-4, Losartan 143809-38-5 143809-39-6
162011-90-7, Rofecoxib 162054-19-5 163303-19-3 163303-25-1
163303-29-5 163303-38-6 163303-55-7 165251-89-8 165328-52-9
169590-41-4, Deracoxib 169951-23-9 169951-24-0 169951-25-1
169951-27-3 169951-28-4 170569-31-0 170569-42-3 170569-50-3
170569-86-5 170569-87-6 170569-88-7 170569-91-2 170570-05-5
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Valdecoxib 181695-81-8 181695-85-2 181696-18-4 181696-33-3
185344-55-2 198470-84-7, Parecoxib 202409-33-4, Etoricoxib
215122-07-9 215122-12-6 215122-14-8 215122-18-2 215122-19-3
215122-20-6 215122-22-8 215122-24-0 215122-27-3 215122-28-4
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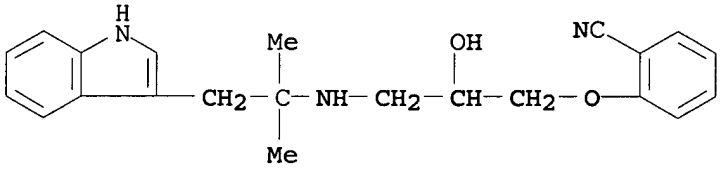
215122-56-8 215122-58-0 215122-59-1 215122-60-4 215122-61-5
215122-62-6 215122-63-7 215122-65-9 215122-71-7 215122-75-1
215122-76-2 215122-77-3 215123-07-2 215123-08-3 215123-16-3
215123-80-1 215123-84-5 266320-83-6 316149-01-6 391894-79-4
391894-80-7 391894-81-8 391894-82-9
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(cyclooxygenase-2 inhibitors and vasomodulators for generalized pain and headache pain treatment)

IT **71119-11-4**, Bucindolol
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(cyclooxygenase-2 inhibitors and vasomodulators for generalized pain and headache pain treatment)

RN 71119-11-4 HCAPLUS
CN Benzonitrile, 2-[2-hydroxy-3-[[2-(1H-indol-3-yl)-1,1-dimethylethyl]amino]propoxy]- (9CI) (CA INDEX NAME)



L44 ANSWER 22 OF 34 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 2001:816726 HCAPLUS
DN 135:355864
TI The CaR receptor as a mediator of migratory cell chemotaxis and/or chemokinesis and methods and compositions for modulating movement of CaR receptor expressing cells
IN Scadden, David T.; Poznansky, Mark C.; Olszak, Ivona T.; Brown, Edward M.
PA The General Hospital Corporation, USA; The Brigham and Women's Hospital, Inc.
SO PCT Int. Appl., 56 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI WO 2001083546 A1 20011108 WO 2000-US15440 20000602
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
US 2002132224 A1 20020919 US 2001-2854 20011101
WO 2003104256 A2 20031218 WO 2002-US35145 20021101
WO 2003104256 A3 20041202
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRAI US 2000-200861P P 20000501
WO 2000-US15440 A2 20000602
US 2001-2854 A 20011101

AB This invention relates to methods and compns. for modulating movement of eukaryotic cells with migratory capacity. More specifically, the invention relates to methods and compns. for modulating movement of **calcium**-sensing receptor (CaR) expressing cells of hematopoietic, neural, epithelial, endothelial, or mesenchymal origin, in a specific site in a subject. The foregoing are useful, inter alia, in the treatment of condictions characterized by a need to modulate migratory-cell movement associated with specific sites in a subject. Specific sites include sites of inflammation and modulation of migratory-cell movement is movement away from an agent source, or repulsion.

IC ICM C07K014-47
ICS C07K014-72; C07K014-435
CC 13-2 (Mammalian Biochemistry)
Section cross-reference(s): 1, 15, **63**
ST **calcium** sensing receptor CaR chemotaxis chemokinesis migratory cell
IT Chemokine receptors
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(CXCR4, enhancing expression of; CaR receptor as mediator of migratory cell chemotaxis and/or chemokinesis and methods and compns. for modulating movement of CaR receptor expressing cells)
IT Chemokines
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(SDF-1 (stromal-derived factor-1), enhancing migration of cell toward; CaR receptor as mediator of migratory cell chemotaxis and/or chemokinesis and methods and compns. for modulating movement of CaR receptor expressing cells)
IT Transplant and Transplantation
(**bone** marrow; CaR receptor as mediator of migratory cell

chemotaxis and/or chemokinesis and methods and compns. for modulating movement of CaR receptor expressing cells)

IT Receptors
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); OCCU (Occurrence); PROC (Process); USES (Uses)
(**calcium**; CaR receptor as mediator of migratory cell chemotaxis and/or chemokinesis and methods and compns. for modulating movement of CaR receptor expressing cells)

IT Chemokine receptors
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(enhancing expression of; CaR receptor as mediator of migratory cell chemotaxis and/or chemokinesis and methods and compns. for modulating movement of CaR receptor expressing cells)

IT Chemokines
Macrophage inflammatory protein 1β
Monocyte chemoattractant protein-1
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(enhancing migration of cell toward; CaR receptor as mediator of migratory cell chemotaxis and/or chemokinesis and methods and compns. for modulating movement of CaR receptor expressing cells)

IT **Bone** marrow
(transplant; CaR receptor as mediator of migratory cell chemotaxis and/or chemokinesis and methods and compns. for modulating movement of CaR receptor expressing cells)

IT Chemokine receptors
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(β chemokine receptor CCR2, enhancing expression of; CaR receptor as mediator of migratory cell chemotaxis and/or chemokinesis and methods and compns. for modulating movement of CaR receptor expressing cells)

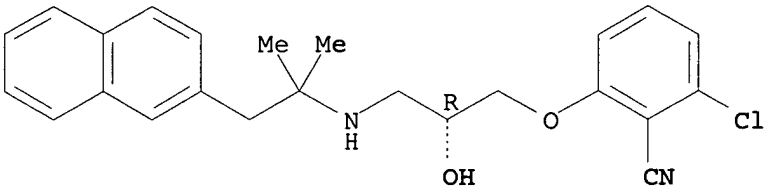
IT Chemokine receptors
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(β chemokine receptor CCR5, enhancing expression of; CaR receptor as mediator of migratory cell chemotaxis and/or chemokinesis and methods and compns. for modulating movement of CaR receptor expressing cells)

IT 7440-70-2, **Calcium**, biological studies 148717-56-0, NPS R-467 148740-52-7, NPS S-467
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(CaR receptor agonist; CaR receptor as mediator of migratory cell chemotaxis and/or chemokinesis and methods and compns. for modulating movement of CaR receptor expressing cells)

IT **284035-33-2**, NPS 2143
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(CaR receptor antagonist; CaR receptor as mediator of migratory cell chemotaxis and/or chemokinesis and methods and compns. for modulating movement of CaR receptor expressing cells)

IT **284035-33-2**, NPS 2143
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(CaR receptor antagonist; CaR receptor as mediator of migratory cell chemotaxis and/or chemokinesis and methods and compns. for modulating movement of CaR receptor expressing cells)
RN 284035-33-2 HCAPLUS
CN Benzonitrile, 2-chloro-6-[(2R)-3-[[1,1-dimethyl-2-(2-naphthalenyl)ethyl]amino]-2-hydroxypropoxy]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

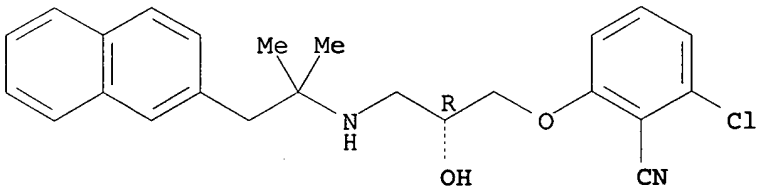


RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 23 OF 34 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 2001:711677 HCAPLUS
DN 136:64048
TI **Calcilytic** compounds: potent and selective Ca2+ receptor antagonists that stimulate secretion of parathyroid hormone
AU Nemeth, Edward F.; Delmar, Eric G.; Heaton, William L.; Miller, Michael A.; Lambert, Lyssa D.; Conklin, Rebecca L.; Gowen, Maxine; Gleason, John G.; Bhatnagar, Pradip K.; Fox, John
CS NPS Pharmaceuticals, Inc., Salt Lake City, UT, USA
SO Journal of Pharmacology and Experimental Therapeutics (2001), 299(1), 323-331
CODEN: JPETAB; ISSN: 0022-3565
PB American Society for Pharmacology and Experimental Therapeutics
DT Journal
LA English
AB Despite the discovery of many ions and mols. that activate the Ca2+ receptor, there are no known ligands that block this receptor. Reported here are the pharmacodynamic properties of a small mol., NPS 2143, which acts as an antagonist at the Ca2+ receptor. This compound blocked (IC50 of 43 nM) increases in cytoplasmic Ca2+ concns. [Ca2+]i elicited by activating the Ca2+ receptor in HEK 293 cells expressing the human Ca2+ receptor. NPS 2143, even when tested at much higher concns. (3 μM), did not affect the activity of a number of other G protein-coupled receptors, including those most structurally homologous to the Ca2+ receptor. NPS 2143 stimulated parathyroid hormone (PTH) secretion from bovine parathyroid cells (EC50 of 41 nM) over a range of extracellular Ca2+ concns. and reversed the effects of the calcimimetic compound NPS R-467 on [Ca2+]i and on secretion of PTH. When infused i.v. in normal rats, NPS 2143 caused a rapid and large increase in plasma levels of PTH. Ca2+ receptor antagonists are termed **calcilytics** and NPS 2143 is the first substance (either atomic or mol.) shown to possess such activity. The pharmacodynamic properties of NPS 2143 together with the recently demonstrated effects of this compound on **bone** formation support the view that orally active **calcilytic** compds. might provide a novel anabolic therapy for **osteoporosis.**

CC 1-12 (Pharmacology)
ST **calcium** receptor antagonist NPS 2143 anabolic **osteoporosis**
IT **Bone** formation
(NPS 2143 as a potent and selective Ca2+ receptor antagonist that stimulate secretion of parathyroid hormone)
IT Receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**calcium**; NPS 2143 as a potent and selective Ca2+ receptor antagonist that stimulate secretion of parathyroid hormone)
IT 7440-70-2, **Calcium**, biological studies 9002-64-6, Parathyroid hormone
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(NPS 2143 as a potent and selective Ca2+ receptor antagonist that stimulate secretion of parathyroid hormone)
IT **284035-33-2**, NPS 2143
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(NPS 2143 as a potent and selective Ca2+ receptor antagonist that stimulate secretion of parathyroid hormone)
IT **284035-33-2**, NPS 2143
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(NPS 2143 as a potent and selective Ca2+ receptor antagonist that stimulate secretion of parathyroid hormone)
RN 284035-33-2 HCAPLUS
CN Benzonitrile, 2-chloro-6-[(2R)-3-[[1,1-dimethyl-2-(2-naphthalenyl)ethyl]amino]-2-hydroxypropoxy]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 24 OF 34 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 2001:545657 HCAPLUS
DN 135:137310
TI [Cyano[[(aryldimethylalkyl)amino]hydroxypropoxy]phenyl]alkanoic acids and analogs useful as **calcilytic** compounds
IN Lago, Amparo M.; Callahan, James Francis; Bhatnagar, Pradip Kumar; Del Mar, Eric G.; Bryan, William M.; Burgess, Joelle L.
PA Smithkline Beecham Corporation, USA; NPS Pharmaceuticals, Inc.
SO PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001053254	A1	20010726	WO 2001-US2402	20010124

W: AE, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CZ, DZ, EE, GE, GH, GM,

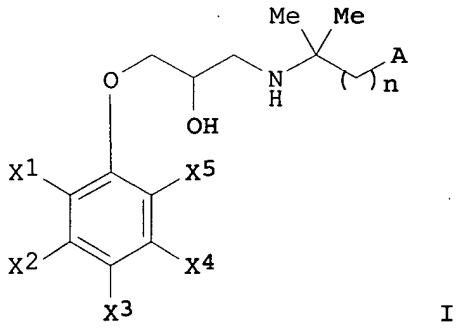
applicants

HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG,
MK, MN, MX, MZ, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, TZ, UA,
US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

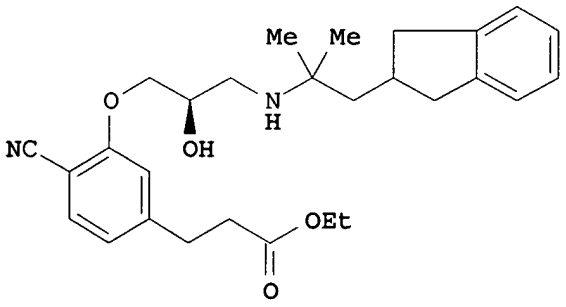
	CA 2397802	AA	20010726	CA 2001-2397802	20010124
	EP 1254106	A1	20021106	EP 2001-910349	20010124
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	BR 2001007592	A	20021119	BR 2001-7592	20010124
	JP 2003520265	T2	20030702	JP 2001-553259	20010124
	AU 764746	B2	20030828	AU 2001-37966	20010124
	NZ 519480	A	20040528	NZ 2001-519480	20010124
	US 2003018203	A1	20030123	US 2002-181338	20020717
	ZA 2002005832	A	20030305	ZA 2002-5832	20020722
	NO 2002003508	A	20020723	NO 2002-3508	20020723
	BG 106942	A	20030131	BG 2002-106942	20020723
	US 2004192741	A1	20040930	US 2004-761986	20040121
PRAI	US 2000-177683P	P	20000124		
	WO 2001-US2402	W	20010124		
	US 2002-181338	B1	20020717		

OS MARPAT 135:137310

GI



I



II

AB Novel **calcilytic** compds. and methods of using them are provided. In particular, compds. I are disclosed [wherein: A = optionally fused (hetero)aryl, dihydro or tetrahydro fused (hetero)aryl, (un)substituted

with any of OH, halo, alkyl, alkoxy, cycloalkyl, CF3, OCF3, cyano, and NO2; X1, X5 = H, halo, cyano, NO2, provided that either X1 or X5 = H; X2, X3, X4 = H, halo, alkoxy, alkyl, or J-K, wherein: J = bond, alkylene, O-alkylene or alkenylene; K = CO2R5, CONR4R4', OH, NR4R4', cyano; R4, R4' = H, alkyl, aryl, heteroaryl; R5 = H, alkyl, or alkyl-(O-alkyl)m-O-alkyl; n = 0-4; m = 1-3; or a pharmaceutically acceptable salt thereof]. The compds. are Ca receptor antagonists, useful for treating diseases or disorders characterized by abnormal **bone** or mineral homeostasis, including **osteosarcoma**, periodontal disease, fracture healing, **osteoarthritis**, rheumatoid arthritis, Paget's disease, humoral hypercalcemia, malignancy, and particularly **osteoporosis**. The compds. may be coadministered with various anti-resorptive agents. Over 20 compds. were prepared and these plus addnl. compds. were claimed. For instance, reaction of (R)-Et 4-cyano-3-(oxiranylmethoxy)benzenepropionate with 2-(indan-2-yl)-1,1-dimethylethylamine (prepns. of both compds. described) gave 63% II, one of the most preferred compds. The most preferred compds. inhibited Ca receptors in vitro with IC50 values of 0.1 μM or less.

IC ICM C07C255-50
ICS A61K031-277

CC 25-24 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
Section cross-reference(s): 1

ST cyanoaryldimethylalkylaminohydroxypropoxyphenylalkanoate prepn **calcilytic** treatment **bone** disease **osteoporosis** ; **calcium** receptor antagonist prepn indan naphthalene tetrahydronaphthalene

IT **Bone**, disease
(Paget's, treatment; preparation of [cyano[[(aryldimethylalkyl)amino]hydroxy propoxy]phenyl]alkanoic acids and analogs useful as **calcilytic** compds. for treatment of **bone** disease)

IT Protein motifs
(SH2 domain, coadministration with src SH2 antagonists; preparation of [cyano[[(aryldimethylalkyl)amino]hydroxypropoxy]phenyl]alkanoic acids and analogs useful as **calcilytic** compds. for treatment of **bone** disease)

IT Receptors
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(**calcium**, antagonists; preparation of [cyano[[(aryldimethylalkyl)amino]hydroxypropoxy]phenyl]alkanoic acids and analogs useful as **calcilytic** compds. for treatment of **bone** disease)

IT Vitronectin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(coadministration with antagonists; preparation of [cyano[[(aryldimethylalkyl)amino]hydroxypropoxy]phenyl]alkanoic acids and analogs useful as **calcilytic** compds. for treatment of **bone** disease)

IT Estrogen receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(coadministration with selective modulators; preparation of [cyano[[(aryldimethylalkyl)amino]hydroxypropoxy]phenyl]alkanoic acids and analogs useful as **calcilytic** compds. for treatment of **bone** disease)

IT Estrogens
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(coadministration with; preparation of [cyano[[(aryldimethylalkyl)amino]hydr oxypropoxy]phenyl]alkanoic acids and analogs useful as **calcilytic** compds. for treatment of **bone** disease)

IT Periodontium

(disease, treatment; preparation of [cyano[[(aryldimethylalkyl)amino]hydroxy propoxy]phenyl]alkanoic acids and analogs useful as **calcilytic** compds. for treatment of **bone** disease)

IT **Bone**, disease
(fracture, treatment; preparation of [cyano[[(aryldimethylalkyl)amino]hydrox ypropoxy]phenyl]alkanoic acids and analogs useful as **calcilytic** compds. for treatment of **bone** disease)

IT Neoplasm
(humoral hypercalcemia of malignancy, treatment; preparation of [cyano[[(aryldimethylalkyl)amino]hydroxypropoxy]phenyl]alkanoic acids and analogs useful as **calcilytic** compds. for treatment of **bone** disease)

IT **Bone**, neoplasm
(**osteosarcoma**, treatment; preparation of [cyano[[(aryldimethylalkyl)amino]hydroxypropoxy]phenyl]alkanoic acids and analogs useful as **calcilytic** compds. for treatment of **bone** disease)

IT Antiarthritics
Antitumor agents
(preparation of [cyano[[(aryldimethylalkyl)amino]hydroxypropoxy]phenyl]alkan oic acids and analogs useful as **calcilytic** compds. for treatment of **bone** disease)

IT **Bone**
(resorption, inhibitors, coadministration with; preparation of [cyano[[(aryldimethylalkyl)amino]hydroxypropoxy]phenyl]alkanoic acids and analogs useful as **calcilytic** compds. for treatment of **bone** disease)

IT **Osteoporosis**
(therapeutic agents; preparation of [cyano[[(aryldimethylalkyl)amino]hydroxy propoxy]phenyl]alkanoic acids and analogs useful as **calcilytic** compds. for treatment of **bone** disease)

IT **Bone**, disease
Bone, neoplasm
Osteoarthritis
Rheumatoid arthritis
(treatment; preparation of [cyano[[(aryldimethylalkyl)amino]hydroxypropoxy]p henyl]alkanoic acids and analogs useful as **calcilytic** compds. for treatment of **bone** disease)

IT 13598-36-2D, Phosphonic acid, alkylidenebis- derivs.
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(bisphosphonate, coadministration with; preparation of [cyano[[(aryldimethylalkyl)amino]hydroxypropoxy]phenyl]alkanoic acids and analogs useful as **calcilytic** compds. for treatment of **bone** disease)

IT 94716-09-3, cathepsin K
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(coadministration with inhibitors of; preparation of [cyano[[(aryldimethylalkyl)amino]hydroxypropoxy]phenyl]alkanoic acids and analogs useful as **calcilytic** compds. for treatment of **bone** disease)

IT 9007-12-9, Calcitonin 32222-06-3, 1,25-Dihydroxyvitamin D3
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(coadministration with; preparation of [cyano[[(aryldimethylalkyl)amino]hydr oxypropoxy]phenyl]alkanoic acids and analogs useful as **calcilytic** compds. for treatment of **bone** disease)

IT **351491-01-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); **PREP (Preparation)**; RACT (Reactant or reagent); USES (Uses)

(drug candidate; preparation of [cyano[[(aryldimethylalkyl)amino]hydroxyprop oxy]phenyl]alkanoic acids and analogs useful as **calcilytic** compds. for treatment of **bone** disease)

IT **246218-78-0P 246218-79-1P 246218-82-6P**
246218-83-7P 246218-84-8P 246218-85-9P
246218-86-0P 246218-87-1P 351490-26-1P
351490-27-2P 351490-28-3P 351490-29-4P
351490-30-7P 351490-31-8P 351490-32-9P
351490-33-0P 351490-34-1P 351490-35-2P
351490-36-3P 351490-37-4P 351490-38-5P
351490-39-6P 351490-40-9P 351490-41-0P
351490-42-1P 351490-43-2P 351490-44-3P
351490-45-4P 351490-46-5P 351490-47-6P
351490-48-7P 351490-49-8P 351490-50-1P
351490-51-2P 351490-52-3P 351490-53-4P
351490-54-5P 351490-55-6P 351490-56-7P
351490-57-8P 351490-58-9P 351490-59-0P
351490-60-3P 351490-61-4P 351490-62-5P
351490-63-6P 351490-64-7P 351490-65-8P
351490-66-9P 351490-67-0P 351490-68-1P
351490-69-2P 351490-70-5P 351490-71-6P
351490-72-7P 351490-73-8P 351490-74-9P
351490-75-0P 351490-76-1P 351490-77-2P
351490-78-3P 351490-79-4P 351490-80-7P
351490-81-8P 351490-82-9P 351490-83-0P
351490-84-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(drug candidate; preparation of [cyano[[(aryldimethylalkyl)amino]hydroxyprop oxy]phenyl]alkanoic acids and analogs useful as **calcilytic** compds. for treatment of **bone** disease)

IT 7440-70-2, **Calcium**, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(humoral hypercalcemia of malignancy, treatment; preparation of [cyano[[(aryldimethylalkyl)amino]hydroxypropoxy]phenyl]alkanoic acids and analogs useful as **calcilytic** compds. for treatment of **bone** disease)

IT 9002-64-6, Parathyroid hormone
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(increasing levels of; preparation of [cyano[[(aryldimethylalkyl)amino]hydro xypropoxy]phenyl]alkanoic acids and analogs useful as **calcilytic** compds. for treatment of **bone** disease)

IT 34708-60-6P 53273-37-3P 246219-43-2P 246219-46-5P 351490-85-2P
351490-86-3P 351490-87-4P 351490-88-5P 351490-89-6P 351490-90-9P
351490-91-0P 351490-93-2P 351490-94-3P 351490-97-6P 351490-98-7P
351490-99-8P **351491-00-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(intermediate; preparation of [cyano[[(aryldimethylalkyl)amino]hydroxypropox y]phenyl]alkanoic acids and analogs useful as **calcilytic** compds. for treatment of **bone** disease)

IT 71-41-0, Pentan-1-ol, reactions 78-92-2, Butan-2-ol 107-98-2, 1-Methoxypropan-2-ol 109-86-4, 2-Methoxyethanol 110-80-5, 2-Ethoxyethanol 123-51-3, 3-Methylbutan-1-ol 542-69-8, 1-Iodobutane 584-02-1, Pentan-3-ol 621-54-5, 3-(3-Hydroxyphenyl)propionic acid 629-27-6, 1-Iodooctane 6482-24-2, 1-Bromo-2-methoxyethane 18997-19-8, Chloromethyl pivalate 24470-78-8, Isopropyltriphenylphosphonium iodide

30084-91-4 37868-26-1, Indan-2-ylacetic acid 75178-90-4 79069-14-0, tert-Butyloxycarbonyl-(S)-valinol 115314-17-5, (2R)-Glycidyl 3-nitrobenzenesulfonate **351490-92-1** 351490-95-4 351490-96-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(precursor; preparation of [cyano[[(aryldimethylalkyl)amino]hydroxypropoxy]phenyl]alkanoic acids and analogs useful as **calcilytic** compds. for treatment of **bone** disease)

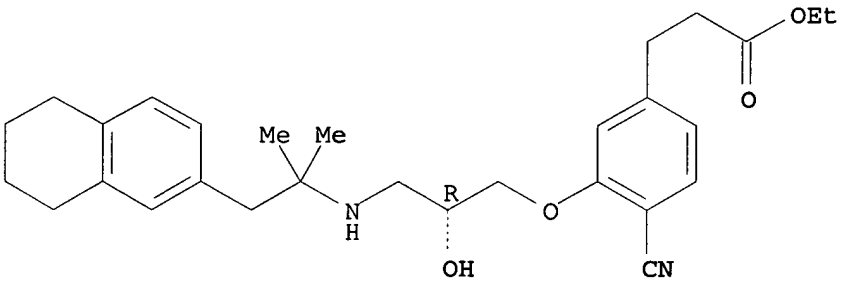
IT 9000-83-3
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(proton-translocating, V-type, coadministration with inhibitors; preparation of [cyano[[(aryldimethylalkyl)amino]hydroxypropoxy]phenyl]alkanoic acids and analogs useful as **calcilytic** compds. for treatment of **bone** disease)

IT 141349-89-5, src protein tyrosine kinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(src SH2 antagonists, coadministration with; preparation of [cyano[[(aryldimethylalkyl)amino]hydroxypropoxy]phenyl]alkanoic acids and analogs useful as **calcilytic** compds. for treatment of **bone** disease)

IT **351491-01-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **PREP (Preparation)**; **THU (Therapeutic use)**; **THU (Therapeutic use)**; **PREP (Preparation)**; **PREP (Preparation)**; RACT (Reactant or reagent); USES (Uses)
(drug candidate; preparation of [cyano[[(aryldimethylalkyl)amino]hydroxypropoxy]phenyl]alkanoic acids and analogs useful as **calcilytic** compds. for treatment of **bone** disease)

RN 351491-01-5 HCAPLUS
CN Benzenepropanoic acid, 4-cyano-3-[(2R)-3-[[1,1-dimethyl-2-(5,6,7,8-tetrahydro-2-naphthalenyl)ethyl]amino]-2-hydroxypropoxy]-, ethyl ester, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 25 OF 34 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 2001:100968 HCAPLUS
DN 134:157570
TI **Calcilytic** compounds for the treatment of **bone** disease
IN Gowen, Maxine; Suva, Larry J.; Fox, John; Stroup, George B.; Nemeth, Edward F.
PA Smithkline Beecham Corporation, USA; NPS Pharmaceuticals, Inc.

SO PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001008673	A1	20010208	WO 2000-US20834	20000731
	W: AE, AL, AU, BA, BB, BG, BR, CA, CN, CZ, DZ, EE, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, TZ, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2380081	AA	20010208	CA 2000-2380081	20000731
	EP 1200076	A1	20020502	EP 2000-952319	20000731
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
	BR 2000012921	A	20020618	BR 2000-12921	20000731
	TR 200200278	T2	20020621	TR 2002-200200278	20000731
	JP 2003505502	T2	20030212	JP 2001-513403	20000731
	AU 764716	B2	20030828	AU 2000-65041	20000731
	NO 2002000466	A	20020320	NO 2002-466	20020129
	ZA 2002000784	A	20030129	ZA 2002-784	20020129
	US 2004214889	A1	20041028	US 2004-852557	20040524
PRAI	US 1999-146778P	P	19990731		
	WO 2000-US20834	W	20000731		
	US 2002-49348	B1	20020130		

AB Methods using **calcilytic** compds. for treating **bone** diseases or disorders are provided. Compds. of the invention include e.g. naphthylethylamine derivs.

IC ICM A61K031-135
CC 1-10 (Pharmacology)
ST **calcilytic** compd **bone** disease; naphthylethylamine deriv **calcilytic** compd **bone** disease
IT **Bone**, disease
(Paget's; **calcilytic** compds. for treatment of **bone** disease)
IT Protein motifs
(SH2 domain, src SH2 antagonists; **calcilytic** compds. for treatment of **bone** disease)
IT Vitronectin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antagonists; **calcilytic** compds. for treatment of **bone** disease)
IT Antitumor agents
(**bone**, metastasis; **calcilytic** compds. for treatment of **bone** disease)
IT Mineral elements, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**bone**; **calcilytic** compds. for treatment of **bone** disease)
IT Anabolic agents
Antiarthritics
Antirheumatic agents
Bone, disease
Drug interactions
Osteoblast

Osteoclast
(**calcilytic** compds. for treatment of **bone** disease)

IT Estrogens
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(**calcilytic** compds. for treatment of **bone** disease)

IT Receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**calcium**; **calcilytic** compds. for treatment of **bone** disease)

IT Periodontium
(disease; **calcilytic** compds. for treatment of **bone** disease)

IT **Bone**, disease
(fracture; **calcilytic** compds. for treatment of **bone** disease)

IT Neoplasm
(humoral hypercalcemia of malignancy; **calcilytic** compds. for treatment of **bone** disease)

IT **Bone**, neoplasm
(metastasis, inhibitors; **calcilytic** compds. for treatment of **bone** disease)

IT **Bone**
(minerals; **calcilytic** compds. for treatment of **bone** disease)

IT Estrogen receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(modulators; **calcilytic** compds. for treatment of **bone** disease)

IT **Bone**, disease
(**osteopenia**; **calcilytic** compds. for treatment of **bone** disease)

IT Joint, anatomical
(replacement; **calcilytic** compds. for treatment of **bone** disease)

IT **Bone**
(resorption, inhibitors; **calcilytic** compds. for treatment of **bone** disease)

IT **Osteoporosis**
(therapeutic agents; **calcilytic** compds. for treatment of **bone** disease)

IT 50-28-2, 17β-Estradiol, biological studies 9007-12-9, Calcitonin 13598-36-2D, Phosphonic acid, bisphosphonates 32222-06-3, 1,25-Dihydroxy-vitamin D3 **198225-86-4 198225-92-2 214624-48-3 246218-79-1 246218-83-7 284035-33-2**, NPS 2143 **324523-20-8 324523-21-9 324523-22-0 324523-23-1 324523-24-2 324523-25-3 324523-26-4 324523-27-5 324523-28-6 324523-29-7 324523-30-0 324523-31-1** 324523-32-2 **324764-49-0**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(**calcilytic** compds. for treatment of **bone** disease)

IT 7440-70-2, **Calcium**, biological studies 9002-64-6, Parathyroid hormone
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(**calcilytic** compds. for treatment of **bone** disease)

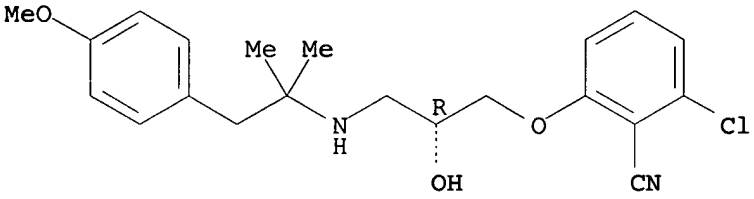
IT 9000-83-3, ATPase 94716-09-3, Cathepsin K
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; **calcilytic** compds. for treatment of **bone** disease)

IT 141349-89-5, Src protein tyrosine kinase 141349-89-5
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(src SH2 antagonists; **calcilytic** compds. for treatment of **bone** disease)

IT **198225-86-4**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(**calcilytic** compds. for treatment of **bone** disease)

RN 198225-86-4 HCAPLUS
CN Benzonitrile, 2-chloro-6-[(2R)-2-hydroxy-3-[[2-(4-methoxyphenyl)-1,1-dimethylethyl]amino]propoxy]-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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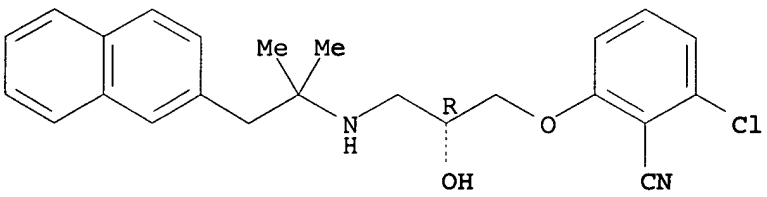
RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 26 OF 34 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 2000:854749 HCAPLUS
DN 134:361205
TI **Calcium** receptor antagonists (**calcilytics**)
AU Nagano, Nobuo
CS Pharmaceutical Development Laboratory, Kirin Brewery Co., Ltd., Japan
SO Clinical Calcium (2000), 10(10), 1252-1254
CODEN: CLCCEJ; ISSN: 0917-5857
PB Iyaku Janarusha
DT Journal
LA Japanese
AB The control of parathyroid hormone secretion by extracellular **calcium** ion is regulated by the parathyroid **calcium** receptor. As receptor antagonists, compds. that inhibit or block the actions of extracellular **calcium** ion at the **calcium** receptor are named **calcilytics.** Daily oral administration of NPS2143, a selective **calcilytic** compound, caused prolonged elevation of plasma parathyroid hormone levels and resulted in a marked increase in **bone** turnover with no net **bone** gain or loss in **osteopenic** ovariectomized rats. Combined administration of NPS2143 and estrogen, an antiresorptive agent, caused an increase in **bone** mass in this animal model. A shorter-acting **calcilytic** compound could provide a novel approach to the treatment of **osteoporosis.**

CC 1-10 (Pharmacology)
ST **calcium** receptor antagonist **calcilytic** NPS2143 antiosteoporotic
IT Estrogens
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(**calcium** receptor antagonists (**calcilytics**) as antiosteoporotics)
IT Receptors
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**calcium**; **calcium** receptor antagonists (**calcilytics**) as antiosteoporotics)
IT **Osteoporosis**
(therapeutic agents; **calcium** receptor antagonists (**calcilytics**) as antiosteoporotics)
IT 9002-64-6, Parathyroid hormone
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**calcium** receptor antagonists (**calcilytics**) as antiosteoporotics)
IT **284035-33-2**, NPS2143
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(**calcium** receptor antagonists (**calcilytics**) as antiosteoporotics)
IT 7440-70-2, **Calcium**, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**calcium** receptor antagonists (**calcilytics**) as antiosteoporotics)
IT **284035-33-2**, NPS2143
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(**calcium** receptor antagonists (**calcilytics**) as antiosteoporotics)
RN 284035-33-2 HCAPLUS
CN Benzonitrile, 2-chloro-6-[(2R)-3-[[1,1-dimethyl-2-(2-naphthalenyl)ethyl]amino]-2-hydroxypropoxy]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

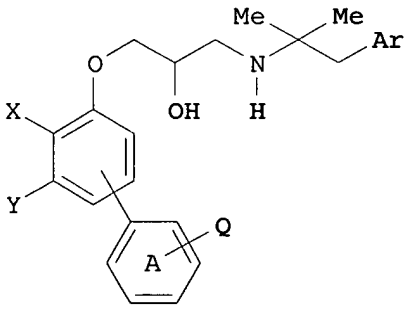


L44 ANSWER 27 OF 34 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 2000:553416 HCAPLUS
DN 133:163944

TI Preparation of substituted 2-hydroxy-3-phenoxypropylamines as **calcilytic** compounds
IN Lago, Amparo M.
PA Smithkline Beecham Corporation, UK
SO PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000045816	A1	20000810	WO 2000-US2676	20000202
	W: AE, AL, AU, BA, BB, BG, BR, CA, CN, CZ, EE, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, TZ, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2361589	AA	20000810	CA 2000-2361589	20000202
	EP 1148876	A1	20011031	EP 2000-913335	20000202
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	BR 2000007922	A	20011106	BR 2000-7922	20000202
	TR 200102244	T2	20011221	TR 2001-200102244	20000202
	JP 2002536330	T2	20021029	JP 2000-596936	20000202
	US 6417215	B1	20020709	US 2001-890310	20010726
	ZA 2001006298	A	20021018	ZA 2001-6298	20010731
	NO 2001003769	A	20010926	NO 2001-3769	20010801
	BG 105847	A	20020430	BG 2001-105847	20010827
PRAI	US 1999-118240P	P	19990202		
	WO 2000-US2676	W	20000202		

OS MARPAT 133:163944
GI

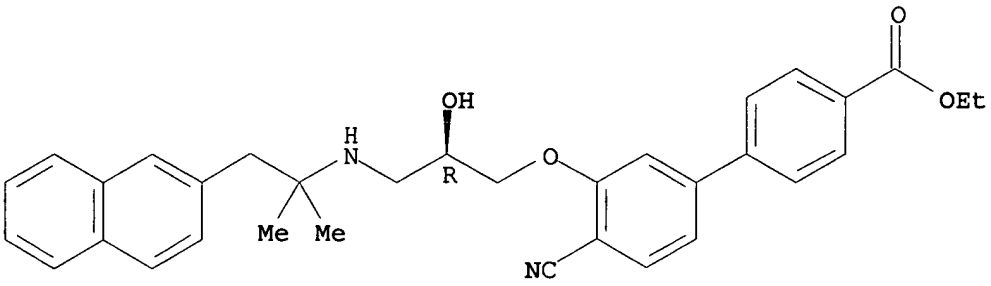


I

AB The title compds. [I; A = aryl attached at 4- or 5-positions; X = CN, NO2, Cl, F, H; Y = Cl, F, Br, I, H; Q = H, R1, SO2R1, CHO, etc.; R1 = H, alkyl; Ar = (un)substituted Ph, naphthyl, heteroaryl, fused heteroaryl] and their salts, useful as **calcium** receptor antagonists, were prepared and formulated. E.g., a multi-step synthesis of (2R)-I.HCl [A ring is attached at 5-position; X = CN, Y = H; Q = 4-CO2Et; Ar = 2-naphthyl] was given. Compds. I are effective at 0.01-100 mg/kg/day.
IC ICM A61K031-41

ICS A61K031-135; C07D257-04; C07C255-00
CC 25-10 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
Section cross-reference(s): 1, **63**
ST hydroxyphenoxypropylamine prepn **calcilytic calcium** channel blocker; phenoxypropylamine hydroxy prepn **calcilytic calcium** channel blocker
IT Receptors
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(**calcium** channel blocker; preparation of substituted 2-hydroxy-3-phenoxypropylamines as **calcilytic** compds.)
IT **288067-22-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); **PREP (Preparation)**; RACT (Reactant or reagent); USES (Uses)
(preparation of substituted 2-hydroxy-3-phenoxypropylamines as **calcilytic** compds.)
IT **288067-23-2P 288067-24-3P 288067-25-4P 288067-26-5P 288067-27-6P 288067-28-7P 288067-29-8P 288067-30-1P 288067-31-2P 288067-32-3P 288067-33-4P 288067-34-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation of substituted 2-hydroxy-3-phenoxypropylamines as **calcilytic** compds.)
IT 611-20-1, 2-Cyanophenol 14047-29-1 40138-16-7, 2-Formylbenzeneboronic acid 105942-08-3 115314-17-5 198226-63-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of substituted 2-hydroxy-3-phenoxypropylamines as **calcilytic** compds.)
IT 40530-18-5P 288067-35-6P 288067-36-7P 288067-37-8P 288067-38-9P 288067-39-0P 288067-40-3P 288067-41-4P **288067-42-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(preparation of substituted 2-hydroxy-3-phenoxypropylamines as **calcilytic** compds.)
IT **288067-22-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **PREP (Preparation)**; **THU (Therapeutic use)**; **THU (Therapeutic use)**; **PREP (Preparation)**; **PREP (Preparation)**; RACT (Reactant or reagent); USES (Uses)
(preparation of substituted 2-hydroxy-3-phenoxypropylamines as **calcilytic** compds.)
RN 288067-22-1 HCAPLUS
CN [1,1'-Biphenyl]-4-carboxylic acid, 4'-cyano-3'-[(2R)-3-[[1,1-dimethyl-2-(2-naphthalenyl)ethyl]amino]-2-hydroxypropoxy]-, ethyl ester, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



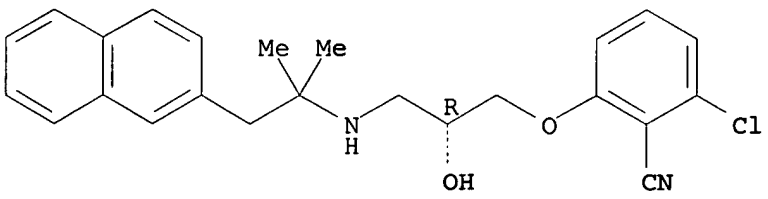
● HCl

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 28 OF 34 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 2000:391550 HCAPLUS
DN 133:99530
TI Antagonizing the parathyroid **calcium** receptor stimulates parathyroid hormone secretion and **bone** formation in **osteopenic** rats
AU Gowen, Maxine; Stroup, George B.; Dodds, Robert A.; James, Ian E.; Votta, Bart J.; Smith, Brian R.; Bhatnagar, Pradip K.; Lago, Amparo M.; Callahan, James F.; DelMar, Eric G.; Miller, Michael A.; Nemeth, Edward F.; Fox, John
CS Department of Bone and Cartilage Biology, SmithKline Beecham Pharmaceuticals, King of Prussia, PA, USA
SO Journal of Clinical Investigation (2000), 105(11), 1595-1604
CODEN: JCINAO; ISSN: 0021-9738
PB American Society for Clinical Investigation
DT Journal
LA English
AB Parathyroid hormone (PTH) is an effective **bone** anabolic agent, but it must be administered parenterally. An orally active anabolic agent would provide a valuable alternative for treating **osteoporosis.** NPS 2143 is a novel, selective antagonist (a "**calcilytic**") of the parathyroid cell Ca2+ receptor. Daily oral administration of NPS 2143 to **osteopenic** ovariectomized (OVX) rats caused a sustained increase in plasma PTH levels, provoking a dramatic increase in **bone** turnover but no net change in **bone** mineral d. Concurrent oral administration of NPS 2143 and s.c. infusion of 17β-estradiol also resulted in increased **bone** turnover. However, the antiresorptive action of estrogen decreased the extent of **bone** resorption stimulated by the elevated PTH levels, leading to an increase in **bone** mass compared with OVX controls or to either treatment alone. Despite the sustained stimulation to the parathyroid gland, parathyroid cells did not undergo hyperplasia. These data demonstrate that an increase in endogenous PTH secretion, induced by antagonism of the parathyroid cell Ca2+ receptor with a small mol., leads to a dramatic increase in **bone** turnover, and they suggest a novel approach to the treatment of **osteoporosis.**
CC 1-12 (Pharmacology)
Section cross-reference(s): 2
ST parathyroid **calcium** receptor antagonism **bone** formation; NPS 2143 **osteoporosis** treatment parathormone

secretion
IT Receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**calcium**; parathyroid **calcium** receptor antagonism with NPS 2143 stimulates parathyroid hormone secretion and **bone** formation in **osteopenic** rats)
IT **Bone** formation
Parathyroid gland
(parathyroid **calcium** receptor antagonism with NPS 2143 stimulates parathyroid hormone secretion and **bone** formation in **osteopenic** rats)
IT **Bone**
(resorption; parathyroid **calcium** receptor antagonism and estradiol increase **bone** turnover in **osteopenic** rats)
IT **Osteoporosis**
(therapeutic agents; parathyroid **calcium** receptor antagonism with NPS 2143 stimulates parathyroid hormone secretion and **bone** formation in **osteopenic** rats)
IT 50-28-2, 17β-Estradiol, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(parathyroid **calcium** receptor antagonism and estradiol increase **bone** turnover in **osteopenic** rats)
IT **284035-33-2**, NPS 2143
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(parathyroid **calcium** receptor antagonism with NPS 2143 stimulates parathyroid hormone secretion and **bone** formation in **osteopenic** rats)
IT 7440-70-2, **Calcium**, biological studies 9002-64-6, Parathormone
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(parathyroid **calcium** receptor antagonism with NPS 2143 stimulates parathyroid hormone secretion and **bone** formation in **osteopenic** rats)
IT **284035-33-2**, NPS 2143
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(parathyroid **calcium** receptor antagonism with NPS 2143 stimulates parathyroid hormone secretion and **bone** formation in **osteopenic** rats)
RN 284035-33-2 HCAPLUS
CN Benzonitrile, 2-chloro-6-[(2R)-3-[[1,1-dimethyl-2-(2-naphthalenyl)ethyl]amino]-2-hydroxypropoxy]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 29 OF 34 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 2000:96006 HCAPLUS
DN 132:151556
TI Preparation of α,α-disubstituted arylalkylamine derivatives as **calcilytic** compounds
IN Del Mar, Eric G.; Barmore, Robert M.; Sheehan, Derek; Van Wagenen, Bradford C.; Callahan, James F.; Keenan, Richard M.; Kotecha, Nikesh R.; Lago, Maria Amparo; Southall, Linda Sue; Thompson, Mervyn
PA NPS Pharmaceuticals, Inc., USA; Smithkline Beecham, Corp.; Smithkline Beecham Plc
SO U.S., 36 pp., Cont.-in-part of U.S. Ser. No. 629,608, abandoned.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6022894	A	20000208	US 1997-832984	19970404
	CA 2251331	AA	19971016	CA 1997-2251331	19970404
	CN 1221401	A	19990630	CN 1997-195368	19970404
	SG 99290	A1	20031027	SG 1999-5132	19970404
	ZA 9702972	A	19980114	ZA 1997-2972	19970408
	TW 483881	B	20020421	TW 1997-86106134	19970508
	US 6521667	B1	20030218	US 1998-132179	19980811
	US 6432656	B1	20020813	US 1999-370097	19990806
	US 2002099220	A1	20020725	US 2001-33001	20011019
	US 6818660	B2	20041116		
	US 2005032850	A1	20050210	US 2004-896614	20040721
PRAI	US 1996-629608	B2	19960409		
	US 1996-32263P	P	19961203		
	US 1997-832984	A3	19970404		
	US 1997-42949P	P	19970407		
	US 1998-132179	A3	19980811		
	US 2001-33001	A3	20011019		

OS MARPAT 132:151556
AB The title compds. R1ZY1CR2R6Y2NHCR3R4Y3R5 [R1 = aryl, alkyl, cycloalkyl; R2 = alkyl, alkoxy, H, etc.; R3, R4 = alkyl; R3R4C = cyclopropyl; R5 = aryl, R6 = H, alkyl, alkenyl, but R6 is not present if R2 is :O; Y1, Y3 = alkylene; R2 = methylene; Z = O, S, alkylene], **calcilytic** agents, were prepared E.g., reaction of 4-chlorophenyl glycidyl ether and 1,1-dimethyl-2-(4-methoxyphenyl)ethylamine gave N-[2-hydroxy-3-(4-chlorophenoxy)propyl]-1,1-dimethyl-2-(4-methoxyphenyl)ethylamine hydrochloride.
IC ICM A61K031-135
INCL 514524000
CC 25-4 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
Section cross-reference(s): 1
ST arylalkylamine prepn **calcilytic** agent; amine arylalkyl prepn **calcilytic** agent
IT Receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)
(**calcium**; preparation of α,α-disubstituted arylalkylamine derivs. as **calcilytic** compds.)
IT 198225-26-2P 198225-29-5P 198225-30-8P 198225-31-9P 198225-33-1P
198225-34-2P 198225-35-3P 198225-36-4P 198225-37-5P 198225-38-6P
198225-39-7P 198225-40-0P 198225-41-1P 198225-42-2P 198225-44-4P

198225-45-5P 198225-46-6P 198225-48-8P 198225-49-9P 198225-50-2P
198225-51-3P 198225-52-4P 198225-53-5P 198225-54-6P
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198225-65-9P 198225-66-0P 198225-67-1P 198225-68-2P 198225-69-3P
198225-70-6P 198225-71-7P 198225-72-8P 198225-73-9P 198225-74-0P
198225-75-1P 198225-76-2P 198225-77-3P 198225-78-4P 198225-79-5P
198225-80-8P 198225-81-9P 198225-82-0P 198225-83-1P 198225-84-2P
198225-85-3P **198225-86-4P** 198225-87-5P 198225-88-6P
198225-89-7P 198225-90-0P 198225-91-1P **198225-92-2P**
198225-93-3P 198225-94-4P **198225-95-5P**
198225-96-6P 198225-97-7P 198225-98-8P **198225-99-9P**
198226-00-5P 198226-01-6P 198226-02-7P 198226-03-8P 198226-04-9P
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198226-10-7P 198226-11-8P 198226-14-1P 198226-16-3P 198226-17-4P
198226-18-5P 198226-19-6P **198226-20-9P** 198226-21-0P
198226-22-1P 198226-23-2P **198226-24-3P** 198226-25-4P
198226-26-5P 198226-27-6P 198226-28-7P 198226-29-8P
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198226-35-6P 198226-36-7P 198226-37-8P 198226-38-9P
198226-39-0P 198226-40-3P 198226-41-4P 198226-42-5P
198226-43-6P 198226-44-7P 198226-45-8P 198226-46-9P
198226-48-1P 198226-49-2P 198287-72-8P **214622-86-3P**
214625-00-0P 257603-55-7P **257603-86-4P** 257603-87-5P
257603-88-6P 257603-89-7P 257603-90-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation of α,α-disubstituted arylalkylamine derivs. as **calcilytic** compds.)

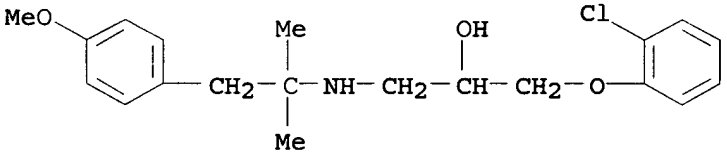
IT 83-56-7, 1,5-Dihydroxynaphthalene 86-52-2, 1-Chloromethylnaphthalene 90-15-3, 1-Naphthol 94-59-7, Safrole 102-48-7, 3,4-Dimethylbenzylamine 104-84-7, 4-Methylbenzylamine 106-89-8, Epichlorohydrin, reactions 106-92-3, Allyl glycidyl ether 122-09-8, 1,1-Dimethyl-2-phenylethylamine 122-60-1, 1,2-Epoxy-3-phenoxypropane 142-84-7, Dipropylamine 372-20-3, 3-Fluorophenol 448-61-3, 2,4,6-Triphenylpyrylium tetrafluoroborate 461-78-9 576-24-9, 2,3-Dichlorophenol 585-45-5 588-63-6, 3-Phenoxypropyl bromide 611-20-1, 2-Cyanophenol 623-05-2, 4-Hydroxybenzyl alcohol 668-45-1, 2-Chloro-6-fluorobenzonitrile 768-56-9, 4-Phenyl-1-butene 824-94-2, 4-Methoxybenzyl chloride 1200-27-7 1730-25-2, Allylmagnesium bromide 1746-13-0, Allyl phenyl ether 1984-59-4, 2,3-Dichloroanisole 2018-90-8, 2-Aminomethylnaphthalene 2186-25-6 2210-74-4 2210-75-5 2210-79-9, Oxirane, (2-methylphenoxymethyl)- 2211-94-1 2211-95-2 2212-04-6 2212-05-7 2404-44-6, 1,2-Epoxydecane 2426-08-6, Butyl glycidyl ether 2461-15-6, 2-Ethylhexyl glycidyl ether 2461-18-9, Dodecyl glycidyl ether 2855-19-8, 1,2-Epoxydodecane 3101-60-8 3290-01-5, 2,3-Dichlorobenzyl chloride 3385-66-8, Octyl glycidyl ether 3497-06-1, Decyl glycidyl ether 4016-14-2, Isopropyl glycidyl ether 4395-73-7, 4-Isopropylbenzylamine 4436-24-2, 2,3-Epoxypropylbenzene 4698-95-7 4812-17-3, 6-Nitro-1-hexene 5002-99-3 5234-06-0, 2-Naphthyl glycidyl ether 5296-21-9, Phenyl glycidyl sulfide 5820-22-4, Methallyl phenyl ether 5926-90-9, Hexyl glycidyl ether 7441-43-2, 4-Ethylbenzylamine 7665-72-7, tert-Butyl glycidyl ether 14133-78-9 15620-80-1 16932-49-3, 2,6-Dimethoxybenzonitrile 18123-82-5 18299-15-5, 4-Hydroxy-3-methylbenzyl alcohol 21324-97-0 23786-14-3, Methyl 4-methoxyphenylacetate 27866-06-4 28446-68-6, 4-Methoxycinnamonitrile 40786-25-2 61396-63-2 62119-49-7 63301-31-5 85721-25-1, 1,2-Epoxy-9-decene 89999-90-6, 3-Chloro-2-cyanophenol 93919-56-3,

4-Trifluoromethoxybenzylamine 115314-14-2 115314-17-5 127102-48-1, Oxiraneoctanol 130187-71-2, 1-Adamantyl glycidyl ether 160778-46-1, 4-Phenylbutyl glycidyl ether 175717-89-2 198226-65-2 198226-66-3 198226-67-4 198226-68-5 198226-69-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of α,α-disubstituted arylalkylamine derivs. as **calcilytic** compds.)

IT 1126-76-7P 2461-42-9P 2489-88-5P 3588-80-5P 4698-94-6P 7470-44-2P, Safrole oxide 15895-57-5P 29206-06-2P 35509-60-5P 37567-54-7P 56490-94-9P 66265-34-7P 67510-95-6P 71590-96-0P 72538-32-0P 79257-73-1P 91552-90-8P 93744-17-3P 100522-09-6P 105254-48-6P 111990-50-2P 134598-06-4P 198225-27-3P 198225-47-7P 198226-53-8P 198226-54-9P 198226-55-0P 198226-56-1P 198226-57-2P 198226-58-3P 198226-59-4P 198226-60-7P 198226-61-8P 198226-62-9P 198226-63-0P 198226-64-1P 214623-85-5P 214623-86-6P 214623-88-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of α,α-disubstituted arylalkylamine derivs. as **calcilytic** compds.)

IT **198225-51-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation of α,α-disubstituted arylalkylamine derivs. as **calcilytic** compds.)

RN 198225-51-3 HCAPLUS
CN 2-Propanol, 1-(2-chlorophenoxy)-3-[[2-(4-methoxyphenyl)-1,1-dimethylethyl]amino]-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

RE.CNT 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

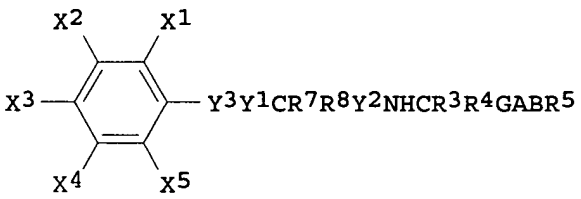
L44 ANSWER 30 OF 34 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 1999:659355 HCAPLUS
DN 131:286273
TI Preparation of hydroxyphenoxypropylnaphthylethylamines, methoxyphenylethylaminophenoxypropanols, and related compounds as **calcilytics.**
IN Bhatnagar, Pradip Kumar; Burgess, Joelle Lorraine; Callahan, James Francis; Calvo, Raul Rolando; Del Mar, Eric G.; Lago, Maria Amparo; Nguyen, Thomas The
PA Smithkline Beecham Corporation, USA; NPS Pharmaceuticals, Inc.
SO PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DT Patent
LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9951569	A1	19991014	WO 1999-US7722	19990408
	W: AE, AL, AU, BA, BB, BG, BR, CA, CN, CZ, EE, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2327279	AA	19991014	CA 1999-2327279	19990408
	AU 9934819	A1	19991025	AU 1999-34819	19990408
	AU 752389	B2	20020919		
	TR 200002896	T2	20010122	TR 2000-200002896	19990408
	EP 1070048	A1	20010124	EP 1999-916516	19990408
	EP 1070048	B1	20050831		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO				
	BR 9909486	A	20011106	BR 1999-9486	19990408
	ZA 200005369	A	20011218	ZA 2000-5369	19990408
	JP 2002510671	T2	20020409	JP 2000-542291	19990408
	NZ 507288	A	20030530	NZ 1999-507288	19990408
	AP 1271	A	20040421	AP 2000-200001931	19990408
	W: GH, GM, KE, LS, MW, MZ, SL, SD, SZ, TZ, UG, ZW				
	AT 303358	E	20050915	AT 1999-916516	19990408
	NO 2000005006	A	20001004	NO 2000-5006	20001004
	US 6395919	B1	20020528	US 2000-647793	20001005
	BG 104916	A	20010629	BG 2000-104916	20001107
PRAI	US 1998-81093P	P	19980408		
	WO 1999-US7722	W	19990408		

OS MARPAT 131:286273

GI



I

AB Title compds. [I; Y1 = bond, (O- or alkyl-substituted) alkylene, alkenylene; Y2 = (alkyl- or haloalkyl-substituted) methylene; Y3 = bond, O, S, imino, alkyleneoxy, alkylenethio, alkyleneimino; R3, R4 = Me, Et; R3R4C = cyclopropyl; R5 = (fused) (substituted) aryl; G = bond, CHR6, CR6; R6 = H, OH, O; R7 = H, OH, alkoxy; R8 = H, alkyl; R7R8 = O; A, B = bond, CH2, NH, O, S, CO; AB = CH:CH, C.tplbond.C; X1, X5 = H, halo, cyano, NO2, alkyl, cycloalkyl, arylmethyl, heteroarylmethyl; X2-X4 = H, halo, alkoxy, aryloxy, heteroaryloxy, arylmethyl, heteroarylmethyl, arylcarbonyl, heteroarylcarbonyl, etc.; with provisos], were prepared as **calcium** receptor antagonists for treatment of abnormal **bone** or mineral homeostasis (no data). Thus, (R)-4-[2-phenyl-2(RS)-(methoxycarbonyl)ethyl]phenoxyglycidol (preparation given), 4-methoxypheny-1,1-dimethylethylamine, and EtNH2 were refluxed 24 h in EtOH to give (R)-1-[1,1-dimethyl-2-(4-methoxyphenyl)ethylamino]-3-[4-(2-phenyl-2-(RS)-methoxycarbonylethyl)phenoxy]propan-2-ol hydrochloride.

IC ICM C07C255-33
CC 25-24 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
Section cross-reference(s): 1
ST hydroxyphenoxypropylnaphthylethylamine methoxyphenylethylaminophenoxypropanol prepn **calcilytic**; **bone** mineral homeostasis disorder treatment hydroxyphenoxypropylnaphthylethylamine methoxyphenylethylaminophenoxypropanol
IT **Bone**, disease
(Paget's, treatment; preparation of hydroxyphenoxypropylnaphthylethylamines, methoxyphenylethylaminophenoxypropanols, and related compds. as **calcilytics**)
IT Receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)
(**calcium**, antagonists; preparation of hydroxyphenoxypropylnaphthylethylamines, methoxyphenylethylaminophenoxy propanols, and related compds. as **calcilytics**)
IT Periodontium
(disease, treatment; preparation of hydroxyphenoxypropylnaphthylethylamines, methoxyphenylethylaminophenoxypropanols, and related compds. as **calcilytics**)
IT **Bone**, neoplasm
(**osteosarcoma**, treatment; preparation of hydroxyphenoxypropylnaphthylethylamines, methoxyphenylethylaminophenoxy propanols, and related compds. as **calcilytics**)
IT Antiarthritics
Antitumor agents
(preparation of hydroxyphenoxypropylnaphthylethylamines, methoxyphenylethylaminophenoxypropanols, and related compds. as **calcilytics**)
IT **Osteoporosis**
(therapeutic agents; preparation of hydroxyphenoxypropylnaphthylethylamines, methoxyphenylethylaminophenoxypropanols, and related compds. as **calcilytics**)
IT Homeostasis
(treatment of disorders of abnormal **bone** or mineral homeostasis; preparation of hydroxyphenoxypropylnaphthylethylamines, methoxyphenylethylaminophenoxypropanols, and related compds. as **calcilytics**)
IT 7440-70-2, **Calcium**, biological studies
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(hypercalcemia, treatment of humoral hypercalcemia; preparation of hydroxyphenoxypropylnaphthylethylamines, methoxyphenylethylaminophenoxy propanols, and related compds. as **calcilytics**)
IT 246218-40-6P 246218-41-7P 246218-42-8P 246218-43-9P 246218-44-0P
246218-45-1P 246218-46-2P 246218-47-3P 246218-48-4P 246218-49-5P
246218-50-8P 246218-51-9P 246218-52-0P 246218-53-1P
246218-54-2P 246218-55-3P 246218-56-4P
246218-57-5P 246218-58-6P 246218-59-7P **246218-60-0P**
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246232-58-6P 246232-61-1P 246234-13-9P 246234-14-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation of hydroxyphenoxypropylnaphthylethylamines, methoxyphenylethylaminophenoxypropanols, and related compds. as **calcilytics**)

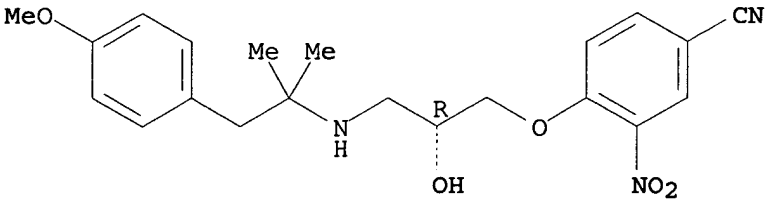
IT 85-44-9, Phthalic anhydride 85-57-4, 2-(4-Hydroxybenzoyl)benzoic acid 89-23-6 97-63-2, Ethyl methacrylate 501-94-0, 4-Hydroxyphenethyl alcohol 621-44-3, 3-Nitro-L-tyrosine 767-00-0, 4-Cyanophenol 1493-27-2, 2-Nitrofluorobenzene 3272-08-0, 4-Hydroxy-3-nitrobenzonitrile 5446-02-6 5597-50-2 10210-17-0 10463-20-4, 4-Hydroxy-3-nitrophenylacetic acid 14191-95-8, 4-Hydroxybenzyl cyanide 14199-15-6, Methyl 4-hydroxyphenylacetate 17138-28-2, Ethyl 4-hydroxyphenylacetate 17362-17-3 23795-02-0 24342-03-8 40530-18-5 41833-13-0, 4-Hydroxy-3-nitrobenzyl alcohol 56490-94-9 60456-23-7 61292-90-8 62889-58-1 77605-57-3 105942-08-3 115314-17-5 123750-60-7 140675-43-0 154872-57-8 198226-63-0 246219-35-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of hydroxyphenoxypropylnaphthylethylamines, methoxyphenylethylaminophenoxypropanols, and related compds. as **calcilytics**)

IT 3116-90-3P 3195-65-1P 77605-63-1P 220936-12-9P 220936-13-0P 246219-16-9P 246219-17-0P 246219-18-1P 246219-19-2P 246219-20-5P 246219-21-6P 246219-22-7P 246219-23-8P 246219-24-9P 246219-25-0P 246219-26-1P 246219-27-2P 246219-28-3P 246219-29-4P 246219-30-7P 246219-31-8P 246219-32-9P 246219-33-0P 246219-34-1P 246219-36-3P 246219-37-4P 246219-38-5P 246219-39-6P 246219-40-9P 246219-41-0P 246219-42-1P 246219-43-2P 246219-44-3P 246219-45-4P 246219-46-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of hydroxyphenoxypropylnaphthylethylamines, methoxyphenylethylaminophenoxypropanols, and related compds. as **calcilytics**)

IT **246218-54-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation of hydroxyphenoxypropylnaphthylethylamines, methoxyphenylethylaminophenoxypropanols, and related compds. as **calcilytics**)

RN 246218-54-2 HCAPLUS
CN Benzonitrile, 4-[(2R)-2-hydroxy-3-[[2-(4-methoxyphenyl)-1,1-dimethylethyl]amino]propoxy]-3-nitro-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 31 OF 34 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 1999:659246 HCAPLUS
DN 131:286417
TI Preparation of N-[hydroxy(chlorocyanophenoxy)propyl]heteroaralkylamines and related compounds as **calcilytics.**
IN Bhatnagar, Pradip Kumar; Callahan, James Francis; Del Mar, Eric G.; Lago, Maria Amparo
PA Smithkline Beecham Corporation, USA; NPS Pharmaceuticals, Inc.
SO PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9951241	A1	19991014	WO 1999-US7760	19990408
	W: AE, AL, AU, BA, BB, BG, BR, CA, CN, CZ, EE, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2327188	AA	19991014	CA 1999-2327188	19990408
	AU 9935513	A1	19991025	AU 1999-35513	19990408
	EP 1069901	A1	20010124	EP 1999-917374	19990408
	R: BE, CH, DE, ES, FR, GB, IT, LI, NL				
	JP 2002510636	T2	20020409	JP 2000-542012	19990408
	US 2002052509	A1	20020502	US 2001-5490	20011204
PRAI	US 1998-81087P	P	19980408		
	WO 1999-US7760	W	19990408		
	US 2000-647794	A1	20001005		

OS MARPAT 131:286417
AB XY3Y1CR7R8Y2NHCR3R4GABR5 [Y1 = bond, (O-or alkyl-substituted) alkylene, alkenylene; Y2 = (alkyl- or haloalkyl-substituted) methylene; Y3 = bond, O, S, imino, alkyleneoxy, alkylenethio, alkyleneimino; R3, R4 = Me, Et; R3R4C = cyclopropyl; R5 = (fused) (substituted) heteroaryl;G = bond, CHR6, CR6; R6 = H, OH, O; R7 = H, OH, alkoxy; R8 = H, alkyl; R7R8 = O; A, B = bond, CH2, NH, O, S, CO; AB = bond, CH:CH, C.tplbond.C; X = specified aminophenyl, aminocarbonylphenyl, aminosulfonylphenyl, etc.; with provisos], were prepared for treatment of abnormal **bone** or mineral homeostasis (no data). Thus, reaction of (R)-3-chloro-2-cyanophenyl glycidyl ether with 3-(2-amino-2-methylpropyl)quinoline (preparation given)

gave (R)-N-[2-hydroxy-3-(3-chloro-2-cyanophenoxy)propyl]-1,1-dimethyl-2-(quinolin-3-yl)ethylamine dihydrochloride.

IC ICM A61K031-535
ICS A01N043-02; A01N043-40; A01N043-42; C07D211-70; C07D211-72; C07D217-12; C07D217-16; C07D217-18; C07D217-38; C07D217-60; C07D307-02

CC 27-17 (Heterocyclic Compounds (One Hetero Atom))

ST hydroxychlorocyanophenoxypropylheteroaralkylamine prepn **calcilytic** ; **bone** mineral disease treatment hydroxychlorocyanophenoxypropyl heteroaralkylamine prepn; **calcium** receptor antagonist hydroxychlorocyanophenoxypropylheteroaralkylamine prepn

IT **Bone**, disease
(Paget's, treatment; preparation of N-[hydroxy(chlorocyanophenoxy)propyl]heteroaralkylamines and related compds. as **calcilytics**)

IT Receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)
(**calcium**, antagonists; preparation of N-[hydroxy(chlorocyanophenoxy)propyl]heteroaralkylamines and related compds. as **calcilytics**)

IT Periodontium
(disease, treatment; preparation of N-[hydroxy(chlorocyanophenoxy)propyl]heteroaralkylamines and related compds. as **calcilytics**)

IT **Bone**, neoplasm
(**osteosarcoma**, treatment; preparation of N-[hydroxy(chlorocyanophenoxy)propyl]heteroaralkylamines and related compds. as **calcilytics**)

IT Antiarthritics
(preparation of N-[hydroxy(chlorocyanophenoxy)propyl]heteroaralkylamines and related compds. as **calcilytics**)

IT **Osteoporosis**
(therapeutic agents; preparation of N-[hydroxy(chlorocyanophenoxy)propyl]heteroaralkylamines and related compds. as **calcilytics**)

IT Homeostasis
(treatment of abnormal **bone** or mineral homeostasis; preparation of N-[hydroxy(chlorocyanophenoxy)propyl]heteroaralkylamines and related compds. as **calcilytics**)

IT **Bone**, disease
(treatment; preparation of N-[hydroxy(chlorocyanophenoxy)propyl]heteroaralkylamines and related compds. as **calcilytics**)

IT 7440-70-2, **Calcium**, biological studies
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(hypercalcemia, treatment of humoral hypercalcemia; preparation of N-[hydroxy(chlorocyanophenoxy)propyl]heteroaralkylamines and related compds. as **calcilytics**)

IT 9002-64-6, Parathyroid hormone
RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)
(increasers of parathyroid hormone levels; preparation of N-[hydroxy(chlorocyanophenoxy)propyl]heteroaralkylamines and related compds. as **calcilytics**)

IT **246154-98-3P 246154-99-4P 246155-00-0P**
246155-01-1P 246155-02-2P 246155-03-3P
246155-04-4P 246155-05-5P 246155-06-6P
246155-07-7P 246155-08-8P 246155-09-9P 246155-10-2P
246155-11-3P 246155-12-4P 246155-13-5P
246155-15-7P 246155-16-8P 246155-17-9P
246155-18-0P 246155-19-1P 246155-20-4P
246155-21-5P 246155-23-7P 246155-24-8P
246155-25-9P 246155-26-0P 246155-27-1P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation of N-[hydroxy(chlorocyanophenoxy)propyl]heteroaralkylamines and related compds. as **calcilytics**)

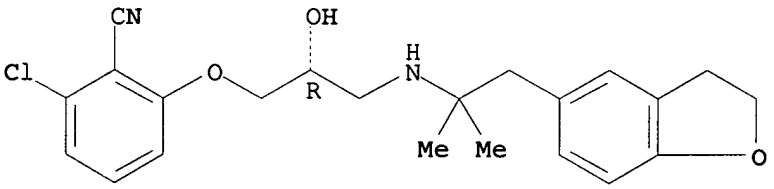
IT 79-46-9, 2-Nitropropane 104-90-5, 5-Ethyl-2-methylpyridine 105-36-2, Ethyl bromoacetate 1530-33-2, Isopropyltriphenylphosphonium bromide 5470-80-4, Isoquinoline-3-carboxaldehyde 5470-96-2, 2-Quinolinecarboxaldehyde 13214-66-9, 4-Phenylbutylamine 13669-42-6, 3-Quinolinecarboxaldehyde 16066-97-0 16386-93-9, 2,2-Dimethyl-4-pentenoic acid 38205-95-7 55745-70-5 120552-94-5 127657-70-9 198226-53-8 246155-33-9 246155-37-3 246155-39-5 246155-40-8 246155-41-9 246155-42-0 246155-44-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of N-[hydroxy(chlorocyanophenoxy)propyl]heteroaralkylamines and related compds. as **calcilytics**)

IT 7521-70-2P, 3-Quinolinemethanamine 204592-26-7P 241134-25-8P 246155-29-3P 246155-30-6P 246155-31-7P 246155-32-8P 246155-34-0P 246155-35-1P 246155-36-2P 246155-43-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of N-[hydroxy(chlorocyanophenoxy)propyl]heteroaralkylamines and related compds. as **calcilytics**)

IT **246154-98-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation of N-[hydroxy(chlorocyanophenoxy)propyl]heteroaralkylamines and related compds. as **calcilytics**)

RN 246154-98-3 HCAPLUS
CN Benzonitrile, 2-chloro-6-[(2R)-3-[[2-(2,3-dihydro-5-benzofuranyl)-1,1-dimethylethyl]amino]-2-hydroxypropoxy]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 32 OF 34 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 1998:682355 HCAPLUS
DN 129:302376
TI Preparation of arylalkylamine as **calcilytic** compounds
IN Barmore, Robert M.; Bhatnagar, Pradip Kumar; Bryan, William M.; Burgess, Joelle Lorraine; Callahan, James Francis; Calvo, Raul Rolando; Del Mar, Eric G.; et al.
PA Smithkline Beecham Corporation, USA; Nps Pharmaceuticals, Inc.
SO PCT Int. Appl., 102 pp.
CODEN: PIXXD2
DT Patent

LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9845255	A1	19981015	WO 1998-US6928	19980408
	W: AL, AU, BA, BB, BG, BR, CA, CN, CZ, EE, GE, HU, ID, IL, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	ZA 9802951	A	19990316	ZA 1998-2951	19980407
	CA 2286454	AA	19981015	CA 1998-2286454	19980408
	AU 9868900	A1	19981030	AU 1998-68900	19980408
	AU 721910	B2	20000720		
	EP 973730	A1	20000126	EP 1998-914581	19980408
	EP 973730	B1	20040616		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI				
	TR 9902516	T2	20000221	TR 1999-9902516	19980408
	BR 9808491	A	20000523	BR 1998-8491	19980408
	JP 2001523223	T2	20011120	JP 1998-543055	19980408
	AT 269300	E	20040715	AT 1998-914581	19980408
	ES 2223126	T3	20050216	ES 1998-914581	19980408
	TW 407144	B	20001001	TW 1998-87105217	19980722
	US 6294531	B1	20010925	US 1999-402310	19991001
	NO 9904877	A	19991007	NO 1999-4877	19991007
PRAI	US 1997-42724P	P	19970408		
	US 1997-61327P	P	19971008		
	US 1997-61329P	P	19971008		
	US 1997-61330P	P	19971008		
	US 1997-61331P	P	19971008		
	US 1997-61333P	P	19971008		
	WO 1998-US6928	W	19980408		

OS MARPAT 129:302376

AB Title compds. XZY1CR7R8Y2NHCR3R4GABR5 [Y1 = covalent bond, alkylene, alkenylene, alkyl; Y2 = methylene, alkyl, CF3; Z = O, S, NH, alkyl, etc.; R3 = CH3, CH3CH2; R4 = CH3, CH3CH2; R3-R4 = cyclopropyl; R5 = C6H5, naphthyl, OH, alkoxy, cycloalkyl, CN, NO2, etc.; G = electron pair, COH, CH, CO; R7 = H, OH, alkoxy; R8 = H, alky; R7-R8 = carbonyl moiety; AB = CH2CH2, CH:CH, CC, covalent bond; X = (un)substituted phenylaminosulfonyl, phenylaminocarbonylalkyl, phenylcarbonylamino, phenylsulfonylamino, etc.] exhibiting **calcilytic** properties are prepared of treating abnormal **bone** or mineral homeostasis (no data).

IC ICM C07C255-07
ICS C07C311-03; C07C229-04; C07C069-76; C07C069-74; C07D223-08; C07D243-12; C07D273-04; C07D265-30; C07D295-092; C07D413-08

CC 23-4 (Aliphatic Compounds)
Section cross-reference(s): 1, **63**

ST arylalkylamine prepn **calcilytic**

IT Resolution (separation)
(Chiralpak AD column diastereoisomers; preparation of arylalkylamine as **calcilytic** compds.)

IT Receptors
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(**calcium**, antagonizing; preparation of arylalkylamine as **calcilytic** compds.)

IT Drug delivery systems
(carriers; preparation of arylalkylamine as **calcilytic** compds.)
IT Alkylation
Bone, disease
Bromination
Cyclization
Dealkylation
Homeostasis
Reduction
(preparation of arylalkylamine as **calcilytic** compds.)
IT Amines, preparation
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of arylalkylamine as **calcilytic** compds.)
IT **214622-39-6P 214622-42-1P 214622-46-5P**
214622-49-8P 214622-51-2P 214622-53-4P
214622-56-7P 214622-60-3P 214622-63-6P
214622-67-0P 214622-72-7P 214622-76-1P
214622-79-4P 214622-83-0P 214622-86-3P
214622-89-6P 214622-93-2P 214622-96-5P
214623-00-4P 214623-03-7P 214623-06-0P
214623-08-2P 214623-12-8P 214623-15-1P
214623-18-4P 214623-20-8P 214623-22-0P
214623-24-2P 214623-26-4P 214623-28-6P
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214623-36-6P 214623-38-8P 214623-39-9P
214623-40-2P 214623-41-3P 214623-42-4P
214623-43-5P 214623-44-6P 214623-45-7P
214623-46-8P 214623-47-9P 214623-48-0P
214623-49-1P 214623-50-4P 214623-51-5P
214623-52-6P 214623-53-7P 214623-54-8P 214623-55-9P
214623-56-0P 214624-48-3P 214624-52-9P
214624-56-3P 214624-60-9P 214624-62-1P
214624-65-4P 214624-68-7P 214624-69-8P
214624-70-1P 214624-71-2P **214624-72-3P**
214624-73-4P 214624-74-5P 214624-75-6P
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214624-79-0P 214624-80-3P 214624-81-4P
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214624-88-1P 214624-89-2P 214624-90-5P
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214624-94-9P 214624-95-0P 214624-96-1P
214624-97-2P 214624-98-3P 214624-99-4P **214625-00-0P**
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214625-07-7P 214625-08-8P 214625-09-9P
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214625-16-8P 214625-17-9P 214625-18-0P
214625-19-1P 214625-20-4P 214625-21-5P
214625-22-6P 214625-23-7P **214625-24-8P**
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214625-28-2P 214625-29-3P 214625-30-6P
214625-31-7P 214625-32-8P 214625-33-9P 214625-34-0P
214625-35-1P 214625-36-2P 214625-37-3P 214625-38-4P 214625-39-5P
214625-40-8P 214625-41-9P 214625-42-0P 214625-43-1P
214625-44-2P 214625-45-3P 214625-46-4P 214625-47-5P 214625-48-6P

214625-49-7P 214625-50-0P 214625-51-1P 214625-52-2P 214625-53-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation of arylalkylamine as **calcilytic** compds.)

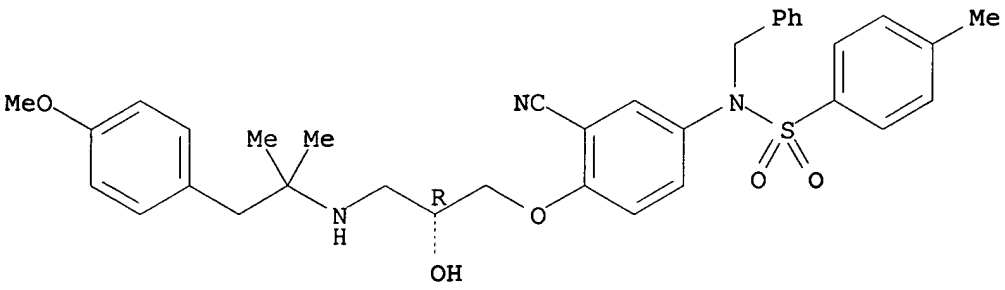
IT 75-08-1, Ethylmercaptan 96-32-2, Methylbromoacetate 98-59-9, 4-Toluenesulfonyl chloride 107-10-8, Propylamine, reactions 110-89-4, Piperidine, reactions 110-91-8, Morpholine, reactions 123-75-1, Pyrrolidine, reactions 123-90-0, Thiomorpholine 124-63-0, Methanesulfonyl chloride 124-68-5 142-84-7, Dipropylamine 668-45-1, 2-Chloro-6-fluorobenzonitrile 765-30-0, Cyclopropylamine 1200-27-7 1493-27-2, 2-Nitrofluorobenzene 1984-59-4, 2,3-Dichloroanisole 5446-02-6 5470-11-1, Hydroxylamine hydrochloride 17417-09-3 25978-74-9, Methyl 3-cyano-4-methoxybenzoate 30525-89-4, Paraformaldehyde 39835-09-1, 2-Cyano-4-nitrophenol 56490-94-9 57260-71-6, tert-Butyl-1-piperazinecarboxylate 58196-47-7, 3-(Cyclopropylamino)propionitrile 115314-17-5, 2R-(-)-Glycidyl-3-nitrobenzenesulfonate 198226-63-0 214624-42-7 214624-43-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of arylalkylamine as **calcilytic** compds.)

IT 6575-10-6P 10496-75-0P 35509-60-5P 53312-81-5P 54584-61-1P 60287-50-5P 60287-51-6P 109803-52-3P 206124-51-8P 206124-52-9P 214623-57-1P 214623-58-2P 214623-59-3P 214623-60-6P 214623-61-7P 214623-62-8P 214623-63-9P 214623-64-0P 214623-65-1P 214623-66-2P 214623-67-3P 214623-68-4P 214623-69-5P 214623-70-8P 214623-71-9P 214623-72-0P 214623-73-1P 214623-74-2P 214623-75-3P 214623-76-4P 214623-77-5P 214623-78-6P 214623-79-7P 214623-80-0P 214623-81-1P 214623-82-2P 214623-83-3P 214623-84-4P 214623-85-5P 214623-86-6P 214623-88-8P 214623-90-2P 214623-93-5P 214623-95-7P 214624-00-7P 214624-02-9P 214624-03-0P 214624-06-3P 214624-07-4P 214624-09-6P 214624-11-0P 214624-13-2P 214624-15-4P 214624-17-6P 214624-19-8P 214624-21-2P 214624-23-4P 214624-25-6P 214624-27-8P 214624-28-9P 214624-30-3P 214624-32-5P 214624-33-6P 214624-35-8P 214624-36-9P 214624-37-0P 214624-38-1P 214624-39-2P 214624-40-5P 214624-41-6P 214624-44-9P 214624-45-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of arylalkylamine as **calcilytic** compds.)

IT **214622-39-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation of arylalkylamine as **calcilytic** compds.)

RN 214622-39-6 HCAPLUS
CN Benzenesulfonamide, N-[3-cyano-4-[(2R)-2-hydroxy-3-[[2-(4-methoxyphenyl)-1,1-dimethylethyl]amino]propoxy]phenyl]-4-methyl-N-(phenylmethyl)-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 33 OF 34 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 1997:684381 HCAPLUS
DN 127:346187
TI Preparation of 1-amino-3-aryloxy-2-propanols and analogs as **calcium** receptor antagonists
IN Van Wagenen, Bradford C.; Del Mar, Eric G.; Sheehan, Derek; Barmore, Robert M.; Keenan, Richard M.; Kotecha, Nikesh R.; Thompson, Mervyn; Callahan, James F.
PA Nps Pharmaceuticals, Inc., USA; Smithkline Beecham Plc; Smithkline Beecham
SO PCT Int. Appl., 123 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9737967	A1	19971016	WO 1997-US5558	19970404
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2251331	AA	19971016	CA 1997-2251331	19970404
AU 9726070	A1	19971029	AU 1997-26070	19970404
AU 726659	B2	20001116		
EP 901459	A1	19990317	EP 1997-917848	19970404
EP 901459	B1	20050629		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
CN 1221401	A	19990630	CN 1997-195368	19970404
BR 9708632	A	20000118	BR 1997-8632	19970404
JP 2001501584	T2	20010206	JP 1997-536327	19970404
SG 99290	A1	20031027	SG 1999-5132	19970404
IL 126458	A1	20040620	IL 1997-126458	19970404
AT 298739	E	20050715	AT 1997-917848	19970404
ZA 9702972	A	19980114	ZA 1997-2972	19970408
TW 483881	B	20020421	TW 1997-86106134	19970508

	US 2002099220	A1	20020725	US 2001-33001	20011019
	US 6818660	B2	20041116		
PRAI	US 1996-629608	A	19960409		
	US 1996-32263P	P	19961203		
	WO 1997-US5558	W	19970404		
	US 1998-132179	A3	19980811		

OS MARPAT 127:346187

AB R1ZZ1CR2R6Z2NHCR3R4Z3R5 [I; R1 = (cyclo)alkyl or aryl; R2 = H, OH, alkyl, alkoxy(carbonyl), etc.; R3,R4 = alkyl; R3R4 = CH2CH2; R5 = (un)substituted Ph or naphthyl; R6 = H or alk(en)yl; R2R6 = O; Z = bond, O, NH, alk(en)ylkene, etc.; Z1 = bond or alk(en)ylkene; Z2,z3 = alkylene] were prepared Thus, 1-naphthol was etherified by epichlorohydrin and the product aminated by H2NCMe2CH2C6H4F-4 to give R1OCH2CH(OH)CH2NHCMe2CH2C6H4F-4. Data for biol. activity of I were given.

IC ICM C07C217-34
ICS C07C217-14; C07C217-28; A61K031-135; A61K031-44; A61K031-395; A61K031-38

CC 25-7 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
Section cross-reference(s): 1

ST aminoaryloxypropanol prepn **calcium** receptor antagonist

IT Receptors
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(**calcium**, mediated disorders; treatment; preparation of 1-amino-3-aryloxy-2-propanols and analogs as **calcium** receptor antagonists)

IT 7440-70-2, **Calcium**, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(extracellular; preparation of 1-amino-3-aryloxy-2-propanols and analogs as **calcium** receptor antagonists)

IT 151136-43-5P 198225-26-2P 198225-27-3P 198225-28-4P 198225-29-5P
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198226-43-6P 198226-44-7P 198226-45-8P 198226-46-9P
198226-48-1P 198226-49-2P **198226-50-5P** 198287-72-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation of 1-amino-3-aryloxy-2-propanols and analogs as **calcium** receptor antagonists)

IT 79-31-2, Isobutyric acid 83-56-7, 1,5-Dihydroxynaphthalene 86-52-2, 1-Chloromethylnaphthalene 90-15-3, 1-Naphthol 94-59-7, Safrole 102-48-7, 3,4-Dimethylbenzylamine 104-84-7, 4-Methylbenzylamine 106-89-8, reactions 106-92-3 122-09-8 122-60-1 372-20-3, 3-Fluorophenol 448-61-3, 2,4,6-Triphenylpyrylium tetrafluoroborate 461-78-9, α,α-Dimethyl-4-chlorobenzeneethanamine 576-24-9, 2,3-Dichlorophenol 585-45-5, 3-TriFluoromethylphenyl glycidyl ether 588-63-6, 3-Phenoxypropyl bromide 600-24-8, 2-Nitrobutane 611-20-1, 2-Cyanophenol 623-05-2, 4-Hydroxybenzyl alcohol 668-45-1, 2-Chloro-6-fluorobenzonitrile 768-56-9, 4-Phenyl-1-butene 824-94-2, 4-Methoxybenzyl chloride 1200-27-7, 1,1-Dimethyl-2-(4-fluorophenyl)ethanamine 1730-25-2 1746-13-0, Allyl phenyl ether 2018-90-8, 2-Aminomethylnaphthalene 2186-25-6, Oxirane, [(3-methylphenoxy)methyl]- 2210-74-4, Oxirane, [(2-methoxyphenoxy)methyl]- 2210-75-5, Oxirane, [(3-methoxyphenoxy)methyl]- 2210-79-9, 2-Methylphenyl glycidyl ether 2211-94-1, Oxirane, [[4-methoxyphenoxy]methyl]- 2211-95-2, Oxirane, [(3-chlorophenoxy)methyl]- 2212-04-6, 2-Chlorophenyl glycidyl ether 2212-05-7, 4-Chlorophenyl glycidyl ether 2404-44-6, 1,2-Epoxydecane 2426-08-6, Butyl glycidyl ether 2461-15-6, 2-Ethylhexyl glycidyl ether 2461-18-9, Dodecyl glycidyl ether 2855-19-8, 1,2-Epoxydodecane 3101-60-8, 4-tert-Butylphenyl glycidyl ether 3132-64-7, Epibromohydrin 3290-01-5, 2,3-Dichlorobenzyl chloride 3385-66-8 3497-06-1 4016-14-2, Isopropyl glycidyl ether 4395-73-7, 4-Isopropylbenzylamine 4436-24-2, 2,3-Epoxypropylbenzene 4698-95-7, Oxirane, [[2-(trifluoromethyl)phenoxy]methyl]- 4812-17-3, 6-Nitro-1-hexene 5002-99-3, Oxirane, [[3-(1,1-dimethylethyl)phenoxy]methyl]- 5234-06-0, 2-Naphthyl glycidyl ether 5296-21-9, Phenyl glycidyl sulfide 5820-22-4, Methallyl phenyl ether 5926-90-9 7441-43-2, 4-Ethylbenzylamine 7665-72-7, tert-Butyl glycidyl ether 14133-78-9 15620-80-1, 2-Fluorophenyl glycidyl ether 16932-49-3, 2,6-Dimethoxybenzonitrile 18123-82-5, 4-Fluorophenyl glycidyl ether 18299-15-5, 4-Hydroxy-3-methylbenzenemethanol 21324-97-0 23786-14-3, Methyl 4-methoxyphenylacetate 27866-06-4 28446-68-6, 4-Methoxycinnamonitrile 40786-25-2, Oxirane, [[2-(1,1-dimethylethyl)phenoxy]methyl]- 61396-63-2 62119-49-7 63301-31-5 85721-25-1 93919-56-3, 4-Trifluoromethoxybenzylamine 103273-65-0, α,α-Dimethyl-3-chlorobenzeneethanamine 115314-14-2 115314-17-5, (R)-Glycidyl 3-nitrobenzenesulfonate 127102-48-1, Oxiraneoctanol 130187-71-2 175717-89-2 198226-65-2 198226-66-3, α,α-Dimethyl-3-methoxybenzeneethanamine 198226-67-4 198226-68-5 198226-69-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 1-amino-3-aryloxy-2-propanols and analogs as **calcium** receptor antagonists)

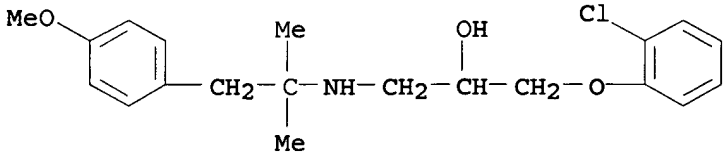
IT 1126-76-7P, 3,4-Epoxybutylbenzene 2461-42-9P, 1-Naphthyl glycidyl ether 2489-88-5P, 1-(3-Butenyl)naphthalene 3588-80-5P, 5-Methoxy-1-naphthol 4698-94-6P, 3-Fluorophenyl glycidyl ether 7470-44-2P, Safrole oxide 15895-57-5P 22442-48-4P, 3-(4-Methoxyphenyl)propionitrile 29206-06-2P 37567-54-7P 56490-94-9P, α,α-Dimethyl-4-methoxybenzeneethanamine 71590-96-0P, 2-Cyano-3-methoxyphenol 76275-47-3P 79257-73-1P 89999-90-6P 91552-90-8P 93744-17-3P 100522-09-6P 105254-48-6P 134598-06-4P 198226-52-7P 198226-53-8P 198226-54-9P 198226-55-0P 198226-56-1P 198226-57-2P 198226-58-3P 198226-59-4P 198226-60-7P 198226-61-8P 198226-62-9P 198226-63-0P

198226-64-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 1-amino-3-aryloxy-2-propanols and analogs as **calcium** receptor antagonists)

IT **198225-51-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation of 1-amino-3-aryloxy-2-propanols and analogs as **calcium** receptor antagonists)

RN 198225-51-3 HCAPLUS

CN 2-Propanol, 1-(2-chlorophenoxy)-3-[[2-(4-methoxyphenyl)-1,1-dimethylethyl]amino]-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

L44 ANSWER 34 OF 34 HCAPLUS COPYRIGHT 2006 ACS on STN

AN 1991:229391 HCAPLUS

DN 114:229391

TI Preparation of tripeptides with N terminal carbamoyl or acyl groups as renin inhibitors

IN Schoen, William R.

PA Merck and Co., Inc., USA

SO Eur. Pat. Appl., 50 pp.
CODEN: EPXXDW

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 347987	A2	19891227	EP 1989-201563	19890615
	EP 347987	A3	19910102		
	R: CH, DE, FR, GB, IT, LI, NL				
	JP 02040398	A2	19900209	JP 1989-155939	19890620
PRAI	US 1988-209749	A	19880620		

OS MARPAT 114:229391

AB Q-A-B-E-G-J [I; Q = amino, HO, alkoxy, etc.; A = CO, OC(O); B, E = α-amino acid residue; G = substituted iminotrimethylenecarbonyl; J = substituted amino, substituted alkoxy, etc.], useful as renin inhibitors (no data) were prepared H2NCMe2CONHCH2CH2CO-Phe-His-NHCHQCH(OH)CH2CO-NHCHMePr (Q = cyclohexylmethyl) was prepared in many steps starting from HO2CCMe2CH2CO2Me and PhCH2OH. I are useful in treatment of hypertension and congestive heart failure and may be formulated with many known diuretics, α- and β-adrenergic blocking agents, Ca channel blockers, vasodilators, and central nervous system agents.

IC ICM C07K005-02

ICS A61K037-64
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, **63**
IT Ion channel blockers
(**calcium**, pharmaceuticals containing renin inhibitors and)
IT 50-55-5, Reserpine 50-60-2, Phentolamine 51-50-3, Dibenamine
52-01-7, Spironolactone 52-53-9, Verapamil 54-31-9, Furosemide
55-65-2, Guanethidine 58-54-8 58-93-5, Hydrochlorothiazide 58-94-6,
Chlorothiazide 59-66-5, Acetazolamide 59-96-1, Phenoxybenzamine
59-98-3, Tolazoline 73-48-3, Bendroflumethiazide 73-49-4, Quinethazone
77-36-1, Chlorthalidone 86-54-4, Hydralazine 90-54-0, Etafenone
91-33-8, Benzthiazide 133-67-5, Trichlormethiazide 135-07-9,
Methyclothiazide 135-09-1, Hydroflumethiazide 346-18-9, Polythiazide
364-98-7, Diazoxide 390-64-7, Prenylamine 396-01-0, Triamterene
555-30-6, Methyldopa 2609-46-3, Amiloride 3416-26-0, Lidoflazine
3930-20-9, Sotalol 4205-90-7, Clonidine 5741-22-0, Moprolol
6621-47-2, Perhexiline 14402-89-2, Sodium nitroprusside 16662-47-8,
Gallopamil 17560-51-9, Metolazone 19216-56-9, Prazosin 21829-25-4,
Nifedipine 22568-64-5, Diacetolol 22664-55-7, Metipranolol
23694-81-7, Mepindolol 26807-65-8, Indapamide 28395-03-1, Bumetanide
30187-90-7, Xibenolol 34915-68-9, Bunitrolol 34919-98-7, Cetamolol
36894-69-6, Labetalol 37517-30-9, Acebutolol 37855-80-4 38304-91-5,
Minoxidil 38363-40-5, Penbutolol 39552-01-7, Befunolol 39562-70-4,
Nitrendipine 39563-28-5, Cloranolol 40180-04-9, Ticrynafen
42200-33-9, Nadolol 42399-41-7, Diltiazem 47082-97-3, Pargolol
51781-06-7, Carteolol 52468-60-7, Flunarizine 53672-88-1 54340-62-4,
Bufuralol 55294-15-0, Muzolimine 55985-32-5, Nicardipine 56049-88-8,
Indacrinone 56980-93-9, Celiprolol 57010-31-8, Tiapamil 57281-35-3
57775-29-8, Carazolol 58409-59-9, Bucumolol 58930-32-8, Butofilolol
59010-44-5, Prizidilol 59170-23-9, Bevantolol 60607-68-3, Indenolol
62571-86-2, Captopril 62658-63-3, Bopindolol 62774-96-3 63659-18-7,
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Nimodipine 66264-77-5, Sulfinalol 66451-06-7, Bornaprolol
66722-44-9, Bisoprolol 67793-71-9 67982-19-8 68377-92-4, Arotinolol
69479-26-1 69907-17-1 70169-23-2 70260-53-6 70958-86-0
71119-11-4, Bucindolol 72509-76-3, Felodipine 72825-08-2
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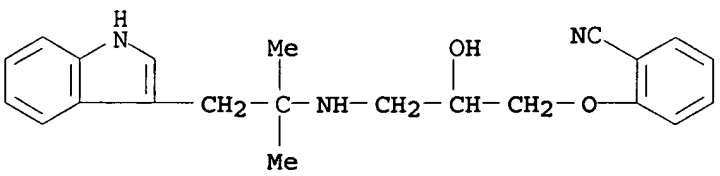
128182-67-2 128182-68-3 128182-69-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(antihypertensive pharmaceuticals containing renin inhibitors and)
IT **71119-11-4**, Bucindolol
RL: RCT (Reactant); RACT (Reactant or reagent)
(antihypertensive pharmaceuticals containing renin inhibitors and)
RN 71119-11-4 HCAPLUS
CN Benzonitrile, 2-[2-hydroxy-3-[[2-(1H-indol-3-yl)-1,1-dimethylethyl]amino]propoxy]- (9CI) (CA INDEX NAME)



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